



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) EP 1 098 626 B1

(12) EUROPEAN PATENT SPECIFICATION

(45) Date of publication and mention of the grant of the patent:
06.05.2004 Bulletin 2004/19

(21) Application number: **99935621.5**

(22) Date of filing: **16.07.1999**

(51) Int Cl.7: **A61K 7/06, A61K 31/19**

(86) International application number:
PCT/US1999/016100

(87) International publication number:
WO 2000/003749 (27.01.2000 Gazette 2000/04)

(54) **METHOD FOR REGULATING HAIR GROWTH**

VERFAHREN ZUR REGELN DES HAARESWACHSTUMS

METHODE DE REGULATION DE LA POUSSE DES CHEVEUX

(84) Designated Contracting States:
DE ES FR GB IT

(30) Priority: **17.07.1998 US 93285 P**

(43) Date of publication of application:
16.05.2001 Bulletin 2001/20

(73) Proprietor: **UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER Dallas, TX 75235-9094 (US)**

(72) Inventors:

- **BRADBURY, James, Barton**
West Chester, OH 45069 (US)
- **SCHAFER, Shari, Joy**
Cincinnati, OH 45249 (US)
- **KACZVINSKY, Joseph, Robert, Jr.**
Cincinnati, OH 45231 (US)
- **BAILEY, Dorothy**
Fairfield, OH 45014 (US)
- **GALE, Celeste, Dawn**
Hamilton, OH 45013 (US)

(74) Representative: **Grünecker, Kinkeldey, Stockmair & Schwanhäusser Anwaltssozietät Maximilianstrasse 58 80538 München (DE)**

(56) References cited:
EP-A- 0 717 983

- **DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US HIRAYAMA, YUTAKA ET AL: "Protein denaturation inhibitors containing triterpenes" retrieved from STN Database accession no. 126:297468 XP002122053 & JP 09 067253 A (LION CORP, JAPAN) 11 March 1997 (1997-03-11)**
- **PATENT ABSTRACTS OF JAPAN vol. 1998, no. 05, 30 April 1998 (1998-04-30) & JP 10 017431 A (POLA CHEM IND INC), 20 January 1998 (1998-01-20)**
- **DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US HAYASHI, KOTAKU ET AL: "Hair growth stimulants containing alpha.-amyrlin triterpenes or extracts of Centella sp. or Prunella sp." retrieved from STN Database accession no. 122:196541 XP002122052 & JP 07 010722 A (HAYASHI KOTAKU, JAPAN; HAYASHI KAZUKO; HAYASHI HIDEYUKI; HAYASHI HIROKI) 13 January 1995 (1995-01-13)**
- **PATENT ABSTRACTS OF JAPAN vol. 009, no. 283 (C-313), 9 November 1985 (1985-11-09) & JP 60 126218 A (OUYOU SEIKAGAKU KENKYUSHO:KK), 5 July 1985 (1985-07-05)**
- **DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US UCHINO, KEIJIRO ET AL: "Cosmetics, pet foods, lipase inhibitors, and foods containing triterpenes" retrieved from STN Database accession no. 129:265186 XP002122054 & JP 10 265328 A (NIPPON FLOUR MILLS CO., LTD., JAPAN) 6 October 1998 (1998-10-06)**

EP 1 098 626 B1

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- DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US TSUJI, KUNIO ET AL: "Hair growth stimulants containing triterpenes" retrieved from STN Database accession no. 127:99526 XP002122145 & JP 09 157139 A (TSUJI, KUNIO, JAPAN; TSUMURA AND CO.; POLA CHEMICAL INDUSTRIES, INC.) 17 June 1997 (1997-06-17)
- DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US OKADA, MASANORI ET AL: "novel saponin extracted from *Polygala senega* as hair tonic and growth stimulant" retrieved from STN Database accession no. 123:208444 XP002122146 & JP 07 133288 A (POLA KASEI KOGYO KK, JAPAN) 23 May 1995 (1995-05-23)
- DATABASE CHEMABS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US OKAZAKI, TOMOMI ET AL: "Hair tonics containing oleanolic acid derivatives" retrieved from STN Database accession no. 107:161369 XP002122147 & JP 62 093215 A (SHISEIDO CO., LTD., JAPAN) 28 April 1987 (1987-04-28)

Description

[0001] The present invention relates to a method for regulating the growth and loss of hair via the use of compositions containing a compound selected from the group consisting of lupane triterpenes, derivatives of lupane triterpenes, derivatives of oleanane triterpenes, derivatives of ursane triterpenes, and salts and mixtures thereof.

BACKGROUND

[0002] Society in general continues to attach a stigma to hair loss. As a result, men and women who suffer from hair loss often experience self-consciousness relating to the condition. Many methods of "curing" hair loss have been disclosed in the literature and several products claiming to regulate hair growth are currently marketed.

[0003] One approach for growing hair involves the much publicized use of minoxidil (Rogaine®)(6-(1-piperidinyl)-2,4-pyrimidinediamine 3-oxide), a potent antihypertensive agent, as a hair growth promoting agent (see U.S. Patents 3,461,461; 3,973,061; 3,464,987; and 4,139,619). Unfortunately, not all people respond to minoxidil and the efficacy level is limited in those individuals who do exhibit a response.

[0004] Finasteride (Propecia®) is another currently marketed product for promoting hair growth. See EP 823436; US 5,670,643; WO 97/15564; and WO 97/15558. Unfortunately, as with minoxidil, not all people respond to finesteride and the efficacy is limited in those people who do exhibit a response. Moreover, the use of finesteride has been associated with reduced libido, teratogenic effects and other side effects in certain individuals.

[0005] Another approach for "curing" hair loss involves a procedure of weaving synthetic or natural hair strands into the remaining hair strands of the subject. Such a procedure is time-consuming, expensive and requires follow-up re-weavings as the weaves loosen and/or the subject's existing hair strands grow. Furthermore, such a procedure does not cure hair loss, but merely masked the condition.

[0006] Another approach for treating hair loss is the use of hair plugs. This procedure involves the transplantation of terminal hair follicles from regions of normal hair growth on the subject's scalp to regions of thinning or no hair growth on the scalp. This procedure is time consuming, expensive and can be painful. Furthermore, the transplanted plugs, at least in the early stages following transplantation, produce an unnatural look to the scalp.

[0007] Thus, there is a need for an easily administered, efficacious agent for treating hair loss in a mammal, which agent has little or no undesirable side effects.

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SUMMARY OF THE INVENTION

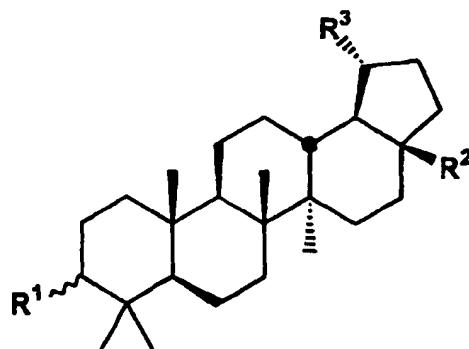
[0008] The present invention relates to a method for regulating hair growth. The method comprises the administration to a human of a composition containing from about 0.00001% to about 99.9% of a compound selected from the group consisting of selected from the group consisting of

a) lupane triterpenes having the structure:

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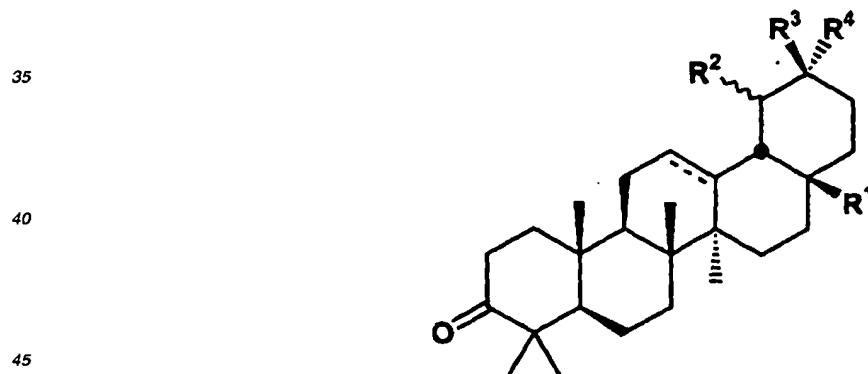
Where R¹ is either

1) connected to the ring system via a single bond, either α - or β - configuration, and is selected from the group consisting of: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; halogen where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated,

substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ or
 10 2) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R⁴,

Where R² is selected from the group consisting of: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of a) cyclic, straight chain
 15 or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii)
 20 OCON(R⁴)₂; and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂,
 25 And where R³ is selected from the group consisting of C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵, or C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, where R⁵ is selected from the group consisting of OH and a halogen,

30 b) compounds having the structure:



where R₁ is selected from the following groups: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of 1) cyclic, straight chain
 35 or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: a) halogens, b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ c) OH, d), OR⁴, e) OCOR⁴, f) OCOOR⁴, g) OCONHR⁴, or h) OCON
 40 (R⁴)₂ and 2) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴,
 45 OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ and 3) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R⁴,

OCOR^4 , OCOOR^4 , OCONHR^4 , or $\text{OCON}(\text{R}^4)_2$;

where $\text{R}_2 = \text{CH}_3$ or H,

where $\text{R}_3 = \text{CH}_3$ or H, and

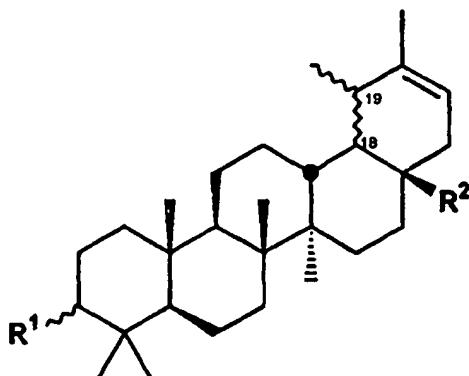
where $\text{R}_4 = \text{CH}_3$ or H; and

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c) derivatives of taraxastane triterpenes having the structure:

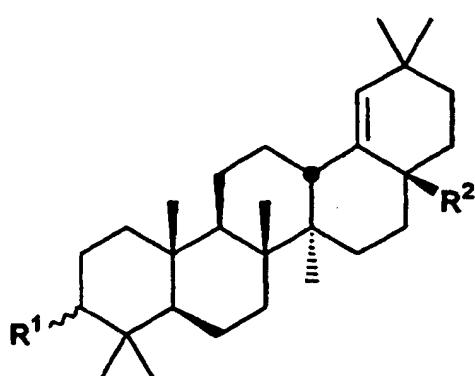
i)

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ii)

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Where R^1 is either

1) connected to the ring system via a single bond, either α - or β - configuration, and is selected from the group consisting of: H, OH, R^4 , OR^4 , OCOR^4 , OCOOR^4 , OCONHR^4 , or $\text{OCON}(\text{R}^4)_2$; halogen where R^4 is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR^4 , OCOR^4 , OCOOR^4 , OCONHR^4 , or $\text{OCON}(\text{R}^4)_2$ iii) OH, iv), OR^4 , v) OCOR^4 , vi) OCOOR^4 , vii) OCONHR^4 , or viii) $\text{OCON}(\text{R}^4)_2$ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR^4 , OCOR^4 , OCOOR^4 , OCONHR^4 , or $\text{OCON}(\text{R}^4)_2$, or
2) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R^4 , and

Where R^2 is selected from the group consisting of: CH_3 , CH_2OH , CH_2OR^4 , CHO, CO_2H , CO_2R^4 , COHNHR^4 , $\text{CON}(\text{R}^4)_2$, CH_2OCOR^4 where R^4 is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR^4 , OCOR^4 , OCOOR^4 , OCONHR^4 , or $\text{OCON}(\text{R}^4)_2$ iii) OH, iv), OR^4 , v) OCOR^4 , vi) OCOOR^4 , vii) OCONHR^4 , or viii) $\text{OCON}(\text{R}^4)_2$.

d) salts of the acid forms of (a), (b) or (c); and

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e) mixtures of (a), (b), (c) or (d).

DETAILED DESCRIPTION OF THE INVENTION

[0009] The present invention relates to a method of regulating hair growth comprising the administration of compositions containing a compound selected from the group consisting of selected from the group consisting of lupane triterpenes, derivatives of lupane triterpenes, salts of lupane triterpene acids, derivatives of oleanane triterpenes, derivatives of ursane triterpenes, and mixtures thereof to a human.

[0010] As used herein, the term "regulating hair growth" means increasing the rate of hair growth and/or inducing the formation of a greater number of hair strands, and/or increasing the diameter of the hair strand, and/or lengthening the hair strand, and/or changing the hair follicle from vellus to terminal, and/or converting follicles from telogen to 10 anagen phase (thereby increasing the overall ratio of anagen phase follicles relative to telogen phase follicles) and/or preventing, retarding, or arresting the process of hair loss, and/or treating alopecia.

[0011] As used herein, "vellus hair follicle" means a hair follicle which produces a soft, short, and often colorless hair fiber. The size of the vellus follicle is considerably smaller than the terminal hair follicle. In an adult, vellus follicles can be found on the forehead (i.e., receding hair line area) and bald scalp.

[0012] As used herein, "terminal follicle" means a hair follicle which produces a coarse, long and often pigmented hair shaft. The size of the terminal follicle is considerably larger, thicker in diameter and longer than the vellus follicle. In an adult, terminal follicles can be found on the scalp, axilla and pubic areas.

[0013] As used herein, "anagen phase" refers to the period in the hair follicle growth cycle wherein the follicle is actively growing and producing new hair.

[0014] As used herein, "telogen phase" refers to the period in the hair growth cycle wherein the follicle is resting and not producing new hair.

[0015] The method of the present invention, including the compositions used therein, is described in detail as follows:

I. THE COMPOSITION

[0016] The compositions of the present invention can be administered topically, orally or parenterally. In a preferred embodiment of the present invention, the compositions of the present invention are administered topically. Topical compositions of the present invention can be in any form, including but not limited to creams, gels, lotions, shampoos, rinses, tonics, sprays, ointments, mousses or pomade. The ingredients comprising the compositions herein, as well 30 as other optional components, are described in detail as follows:

A. The Compound

[0017] The method of the present invention utilizes compositions which contain from about 0.00001% to about 99.9%, preferably from about 0.001 to about 75%, more preferably from about 0.001% to about 50%, even more preferably from about 0.01% to about 25% and most preferably from about 0.1% to about 15% of a compound selected from the group of lupane triterpene acids, certain derivatives of lupane triterpenes, certain derivatives of oleanane triterpenes, certain derivatives of ursane triterpenes, certain derivatives of taraxastane triterpenes and salts and mixtures thereof.

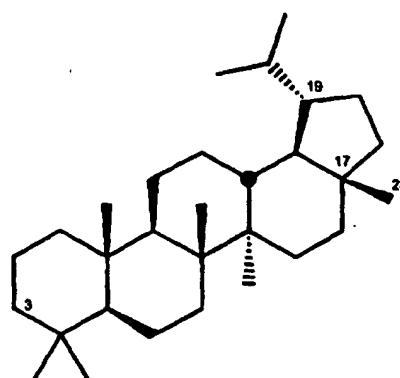
[0018] Lupane triterpenes have the general structure:

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[0019] The term "derivatives of lupane triterpenes" as used herein includes compounds which have additional substituents on this skeleton, double bonds in place of single bonds, changes in stereochemistry or relocated methyls and/

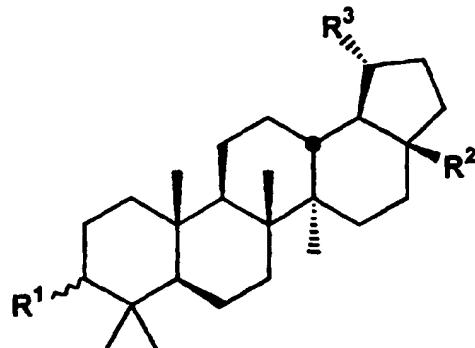
or isopropyl groups.

[0020] Preferred lupane triterpenes and lupane triterpene derivatives of the present invention are those represented by the structure:

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Where R¹ is either

1) connected to the ring system via a single bond, either α - or β - configuration, and is selected from the group consisting of: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; halogen where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂, or
2) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R⁴,

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[0021] Where R² is selected from the group consisting of: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

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[0022] And where R³ is selected from the group consisting of C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵, or C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, where R⁵ is selected from the group consisting of OH and a halogen,

[0023] Preferably, if R⁴ comprises an alkyl group, the alkyl group is unsubstituted.

[0024] Preferably R¹ is selected from the group consisting of H, OH, OCOOR⁴ and OCON(R⁴)₂

[0025] Preferably R² is selected from the group consisting of CH₃, CH₂OH, CH₂OR⁴, CHO, COHNR⁴, and CON(R⁴).

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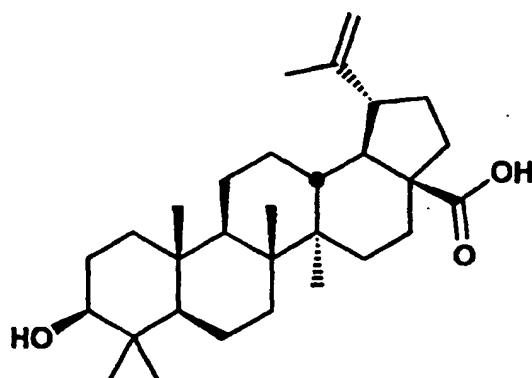
[0026] Especially preferred lupane triterpenes for use herein include betulinic acid, betulonic acid, betulin and derivatives and salts and mixtures thereof. Betulinic acid, betulonic acid and mixtures thereof are most preferred for use herein.

[0027] Betulinic acid has the following structure:

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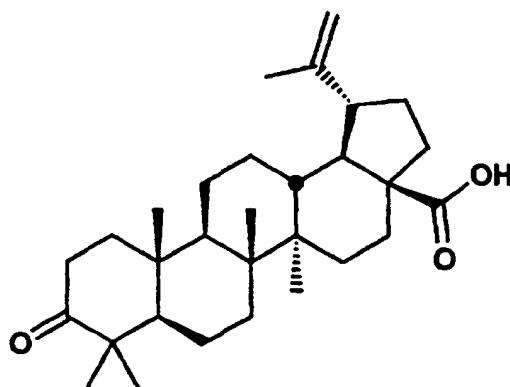
Acacia	Acanthopanax	Aconitum	Acotrema
Actinobale	Adansonia	Adina	Agrostistachys
Ailanthus	Akania	Alangium	Alchemilla
Aleurites	Alnus	Alphitoxolide	Amanoa
Ammannia	Amorphophallus	Ampelozizyphus	Amsonia
Anaxeton	Anemone	Anticharis	Arbutus
Arctostaphylos	Artocarpus	Aspidixia	Avicennia
Bauhinia	Bencomia	Betula	Bischofia
Boehmeria	Bonnetia	Bowdichia	Bretschneidera
Broussonetia	Buxus	Byrsinima	Caesalpinia
Calicarpa	Callicarpa	Callistemon	Calophyllum
Camptotheca	Canthium	Caraipa	Casearia
Cassia	Cassinia	Ceanothus	Celosia
Cerberiopsis	Chamaecrista	Chisocheton	Clerodendron
Clinopodium	Clusia	Coccobola	Coleus
Colubrina	Corchoros	Comus	Cotoneaster
Cottonrose	Crataeva	Crossopteryx	Crotalaria
Curatela	Cylicodiscus	Dendriopoterium	Dendrocalamus
Derris	Dichrostachys	Dicoma	Digera
Dillenia	Diospyros	Dipterocarpus	Discaria
Doliocarpus	Dryobalanops	Duboisia	Echinops
Ehretia	Emmenospermum	Engelhardtia	Enkianthus
Enterolobium	Epigaea	Epilobium	Epithelantha
Eryngium	Erythrospermum	Eucalyptus	Euclea
Eucommia	Eugenia	Euphorbia	Euptelea
Eurya	Fagonia	Fagus	Ficus
Formosia	Forsythia	Fraxinus	Gardenia
Gaultheria	Givotia	Glycyrrhiza	Gochnatia
Gypsophila	Hedyotis	Helicteres	Heliotropium
Hippophae	Hoffmannia	Holoptelea	Hydnocarpus
Hypericum	Hyptis	Inga	Iris
Jacaranda	Jasminum	Juglans	Kayea
Koompassia	Lantana	Lavandula	Lawsonia
Lepechinia	Leptospermum	Lespedeza	Leucothoe

(continued)

	Liana	Licania	Limnophila	Linaria
5	Liquidambar	Lithocarpus	Lusia	Lychnophora
	Lycopus	Lythrum	Madhuca	Maytenus
	Melaleuca	Melanoxylon	Melastoma	Melilotus
	Menyanthes	Mesua	Micromeria	Mimusops
10	Mitrephora	Monttea	Morus	Myodocarpus
	Nelumbo	Nerium	Nymphoides	Nyssa
	Olea	Oplopanax	Origanum	Paeonia
	Pavonia	PediJanthus	Phellinus	Phyllanthus
	Phyllodoce	Physochlaina	Picramnia	Pieris
15	Platyphylla	Plumeria	Polygonum	Pongamia
	Pouteria	Prunella	Psychotria	Putoria
	Pygeum	Pyracantha	Pyrus	Quercus
	Relhania	Rhododendron	Rosa	Rosmarinus
	Roylea	Salvia	Sapium	Sarracenia
20	Schefflera	Schleichera	Schrebera	Scirpus
	Sclerolobium	Scolapia	Scoparia	Senecio
	Senna	Shorea	Solanum	Sorocea
	Sphagnum	Spiraea	Spondianthus	Symplocus
	Syzigium	Tabebuia	Tacca	Talguenea
25	Tectona	Tephrosia	Terminalia	Tetracera
	Tinospora	Tovomita	Transcaucasian	Triadenum
	Tripetaleia	Tripetalia	Triphyophyllum	Tu-Jin-Pi
	Vauquelinia	Vellozia	Viscum	Vismia
	Visnea	Vitis	Vochysia	Wisteria
30	Woodfordia	Wormia	Zizyphus	

[0029] Betulonic acid has the following structure:

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40

45

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[0030] Betulonic acid may be obtained commercially as pure betulonic acid, can be synthesized according to known methods or can be extracted from a plant which contains betulonic acid.

[0031] The following are nonlimited examples of genera of plants which may contain betulonic acid:

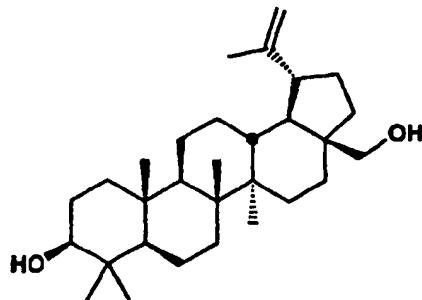
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Acanthopanax	Akania	Alphitonia	Anisomeles
Betula	Boronia	Bursera	Cacosmia
Chisocheton	Dillenia	Dipterocarpus	Duboisia

(continued)

5	Elaeodendron Flacourtiaceae Liquidambar Rhododendron Vellozia	Eucalyptus Glochidion Maytenus Rhodomyrtus Viburnum	Euonymus Helichrysum Orthopterygium Roylea Zizyphus	Euphorbiaceae Lantana Quercus Symphyopappus
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10 [0032] Betulin has the following structure:

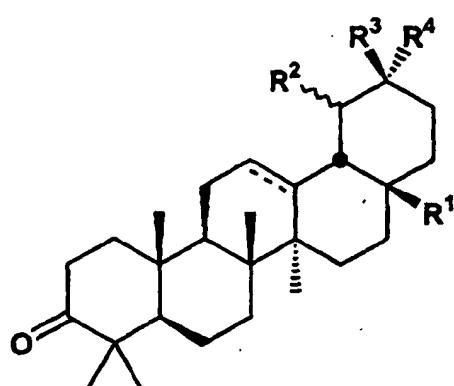


25 [0033] Betulin can be obtained commercially as pure betulin, can be synthesized according to known methods or can be extracted from plants which contain betulin. Nonlimiting examples of genuses of plants which may contain betulin are those listed herein above for betulinic acid.

30 [0034] The plant extracts containing lupane triterpene are extracted by organic solvent extracts, e.g., hexane extracts, chloroform extracts, alcoholic extracts, ethyl acetate extracts, propylene glycol extracts, ethylene glycol extracts, and ether extracts

35 [0035] Extraction procedures for extracting the plant extracts are well known to persons skilled in the art. Extraction can be carried out on a crushed material, which is introduced into the extraction solvent. The extraction can be repeated several times until the material is used up, in accordance with procedures which are well known to persons skilled in the art. The extraction can be carried out at room temperature, or with heating, notably with reflux of the solvent. The proportion by weight between the solvent and the material to be extracted can vary within broad limits and can be, for example, between 1:1 and 10:1.

40 [0036] Certain derivatives of oleanane triterpenes and ursane triterpenes can also be desirably incorporated into the compositions of the present invention. Such derivatives have the structure:



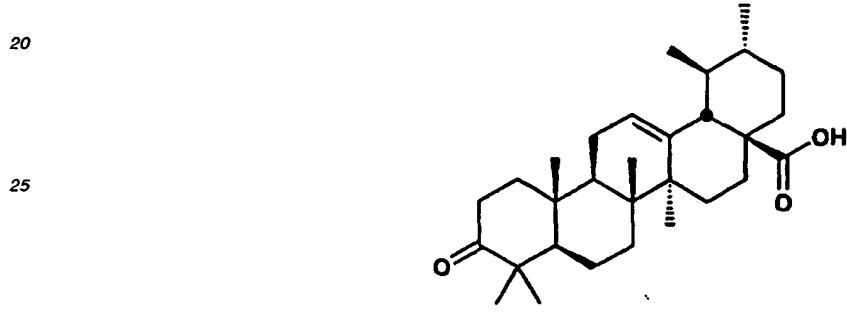
55 where R_1 is selected from the following groups: CH_3 , CH_2OH , CH_2OR^4 , CHO , CO_2H , CO_2R^4 , $COHNR^4$, $CON(R^4)_2$, CH_2OCOR^4 where R^4 is independently selected from the group consisting of a) cyclic, straight chain or branched

chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

where R₂ = CH₃ or H,
where R₃ = CH₃ or H, and
where R₄ = CH₃ or H.

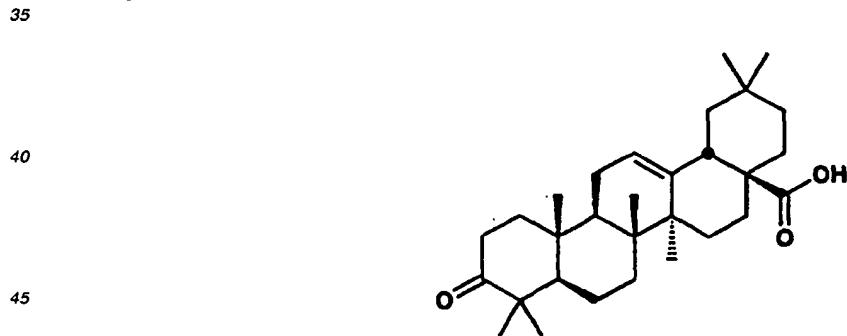
[0037] Preferred derivatives of oleanane triterpenes and ursanes triterpenes are ursonic acid (3-oxo-urs-12-en-28-oic acid) and oleanonic acid (3-oxo-olean-12-en-28-oic acid) and mixtures thereof.

[0038] Ursonic acid has the structure:



[0039] Ursonic acid can be obtained commercially as 100% ursonic acid, can be synthesized according to known methods or can be extracted from plants which contain ursonic acid

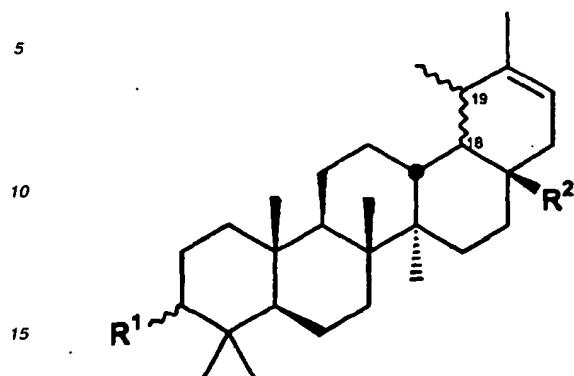
[0040] Oleanonic acid has the structure:



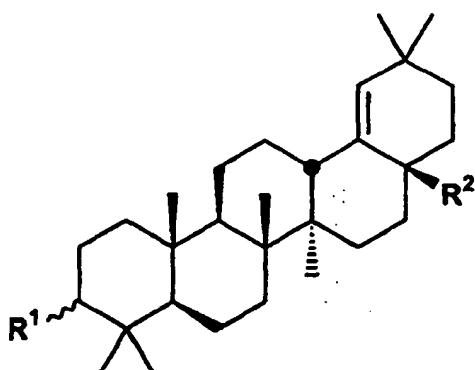
[0041] Oleanonic acid can be obtained commercially as 100% oleanonic acid, can be synthesized according to known methods or can be extracted from plants which contain oleanonic acid.

[0042] Derivatives of taraxastane triterpenes can also be desirably be used in the compositions used in the method of the present invention. Derivatives of taraxastane triterpenes suitable for use herein have the structure:

a)



b)



Where R¹ is either

20 1) connected to the ring system via a single bond, either α - or β - configuration, and is selected from the group consisting of: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; halogen where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂, or
25 2) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R⁴, and
30
35

[0043] Where R² is selected from the group consisting of: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂.

[0044] Suitable salts of the triterpene acids described herein which are suitable for use herein include ammonium, organic amines (e.g., alkylamines, wherein the alkyl group is linear, branched or cyclic), and metal salts. Specific nonlimiting examples of suitable salts for use herein include ammonium, isopropyl amine, morpholine, piperidine, sodium, potassium, calcium, magnesium, zinc, aluminum, and copper salts.

B. Optional ingredients

[0045] The compositions utilized in the method of the present invention can desirably contain a variety of optional ingredients in addition to the compound hereinbefore described in detail.

1. Vehicle

[0046] The compositions which are utilized in the method of the present invention preferably also contain a solid, semi-solid or liquid cosmetically or pharmaceutically acceptable vehicle to act as a diluent, dispersant or carrier for the active components in the composition. As used herein, "pharmaceutically-acceptable" means that drugs, medications

or inert ingredients which the term describes are suitable for use in humans and lower animals without undue toxicity, incompatibility, instability, irritation, allergic response, and the like. As used herein, "cosmetically acceptable" means that ingredients which the term describes are suitable for use in contact with the skin or hair of humans and lower animals without undue toxicity, incompatibility, instability, irritation, allergic response and the like. The cosmetically or pharmaceutically acceptable vehicles comprise from about 0.1% to about 99.99%, preferably from about 25% to about 99.99%, more preferably from about 50% to about 99.99%, even more preferably from about 75% to about 99.9%, most preferably from about 85% to about 99.9% by weight of the composition.

[0047] Acceptable vehicles include, for example, water, lipophilic or hydrophilic emollients/ humectants, surfactants, thickeners, powders, polymers, resins, plasticizers, fillers, lubricants, binders, disintegrants, solvents, co-solvents, buffer systems, preservatives, sweetening agents, flavoring agents, pharmaceutical grade dyes and pigments.

a. Water

[0048] Water can be employed in the compositions herein as a vehicle. When water is employed as the vehicle, the composition will be in the form of an emulsion, suspension or cream.

b. Lipophilic or Hydrophilic Emollients/Humectants

[0049] Hydrophilic or lipophilic emollients and/or humectants can be incorporated into the compositions herein as the vehicle at levels ranging from about 0.5% to about 85%, preferably from about 5% to about 50%, more preferably from about 10% to about 30% by weight of the composition. Suitable emollients and humectants are listed in CTFA Cosmetic Ingredient Handbook, Second Edition, 1992, pp. 572-575. Suitable emollients/humectants include esters, fatty acids and alcohols, polyols, hydrocarbons, silicones, waxes, triglycerides, cationic and nonionic polymers and mixtures thereof.

25

i. Esters

[0050] C1-C30 alcohol esters of C1-C30 carboxylic acids and of C2-C30 dicarboxylic acids, including straight and branched chain materials as well as aromatic derivatives can also be used herein. Also useful are esters such as monoglycerides of C1-C30 carboxylic acids, diglycerides of C1-C30 carboxylic acids, triglycerides of C1-C30 carboxylic acids, ethylene glycol monoesters of C1-C30 carboxylic acids, ethylene glycol diesters of C1-C30 carboxylic acids, propylene glycol monoesters of C1-C30 carboxylic acids, and propylene glycol diesters of C1-C30 carboxylic acids. Straight chain, branched chain and aryl carboxylic acids are included herein. Also useful are propoxylated and ethoxylated derivatives of these materials. Nonlimiting examples include diisopropyl sebacate, diisopropyl adipate, isopropyl myristate, isopropyl palmitate, myristyl propionate, ethylene glycol distearate, 2-ethylhexyl palmitate, isodecyl neopen-tanoate, di-2-ethylhexyl maleate, cetyl palmitate, myristyl myristate, stearyl stearate, cetyl stearate, behenyl behenate, dioctyl maleate, dioctyl sebacate, diisopropyl adipate, cetyl octanoate, diisopropyl dilinoleate, caprylic/capric triglyceride, PEG-6 caprylic/capric triglyceride, PEG-8 caprylic/capric triglyceride, and mixtures thereof.

[0051] Also useful are various C1-C30 monoesters and polyesters of sugars and related materials. These esters are derived from a sugar or polyol moiety and one or more carboxylic acid moieties. Depending on the constituent acid and sugar, these esters can be in either liquid or solid form at room temperature. Examples of liquid esters include: glucose tetraoleate, the glucose tetraesters of soybean oil fatty acids (unsaturated), the mannose tetraesters of mixed soybean oil fatty acids, the galactose tetraesters of oleic acid, the arabinose tetraesters of linoleic acid, xylose tetralinoleate, galactose pentaoleate, sorbitol tetraoleate, the sorbitol hexaesters of unsaturated soybean oil fatty acids, xylitol pentaoleate, sucrose tetraoleate, sucrose pentaoleate, sucrose hexaoleate, sucrose heptoleate, sucrose octaoleate, and mixtures thereof. Examples of solid esters include: sorbitol hexaester in which the carboxylic acid ester moieties are palmitoleate and arachidate in a 1:2 molar ratio; the octaester of raffinose in which the carboxylic acid ester moieties are linoleate and behenate in a 1:3 molar ratio; the heptaester of maltose wherein the esterifying carboxylic acid moieties are sunflower seed oil fatty acids and lignocerate in a 3:4 molar ratio; the octaester of sucrose wherein the esterifying carboxylic acid moieties are oleate and behenate in a 2:6 molar ratio; and the octaester of sucrose wherein the esterifying carboxylic acid moieties are laurate, linoleate and behenate in a 1:3:4 molar ratio. A preferred solid material is sucrose polyester in which the degree of esterification is 7-8, and in which the fatty acid moieties are C18 mono- and/or di-unsaturated and behenic, in a molar ratio of unsaturates:behenic of 1:7 to 3:5. A particularly preferred solid sugar polyester is the octaester of sucrose in which there are about 7 behenic fatty acid moieties and about 1 oleic acid moiety in the molecule. Other materials include cottonseed oil or soybean oil fatty acid esters of sucrose. The ester materials are further described in, U.S. Patent No. 2,831,854, U.S. Patent No. 4,005,196, to Jandacek, issued January 25, 1977; U.S. Patent No. 4,005,195, to Jandacek, issued January 25, 1977, U.S. Patent No. 5,306,516, to Letton et al., issued April 26, 1994; U.S. Patent No. 5,306,515, to Letton et al., issued April 26, 1994;

U.S. Patent No. 5,305,514, to Letton et al., issued April 26, 1994; U.S. Patent No. 4,797,300, to Jandacek et al., issued January 10, 1989; U.S. Patent No. 3,963,699, to Rizzi et al., issued June 15, 1976; U.S. Patent No. 4,518,772, to Volpenhein, issued May 21, 1985; and U.S. Patent No. 4,517,360, to Volpenhein, issued May 21, 1985.

5 ii. Fatty Alcohols and Fatty Acids

[0052] Suitable fatty alcohols and acids include those compounds having from 10 to 20 carbon atoms. Especially preferred are such compounds as cetyl, myristyl, palmitic and stearyl alcohols and acids.

10 iii. Polyols

[0053] Among the polyols which are useful as a vehicle herein are linear and branched chain alkyl polyhydroxyl compounds. Preferred polyols include propylene glycol, sugars having up to about 12 carbons atoms, sugar alcohols having up to about 12 carbon atoms, and mixtures thereof, glycerin, polypropylene glycols, polyethylene glycols, ethyl hexane diol, hexylene glycols, ureas and mixtures thereof.

[0054] Specific examples of useful polyols include materials such as urea; guanidine; glycolic acid and glycolate salts (e.g. ammonium and quaternary alkyl ammonium); lactic acid and lactate salts (e.g. ammonium and quaternary alkyl ammonium); sucrose, fructose, glucose, eruthrose, erythritol, sorbitol, mannitol, glycerol, hexanetriol, propylene glycol, butylene glycol, hexylene glycol, and the like; polyethylene glycols such as PEG-2, PEG-3, PEG-30, PEG-50, polypropylene glycols such as PPG-9, PPG-12, PPG-15, PPG-17, PPG-20, PPG-26, PPG-30, PPG-34; alkoxylated glucose; hyaluronic acid; and mixtures thereof. Also useful are materials such as aloe vera in any of its variety of forms (e.g., aloe vera gel), chitin, starch-grafted sodium polyacrylates such as Sanwet (RTM) IM-1000, IM-1500, and IM-2500 (available from Celanese Superabsorbent Materials, Portsmouth, VA); lactamide monoethanolamine; acetamide monoethanolamine; and mixtures thereof. Also useful are propoxylated glycerols as described in propoxylated glycerols described in U.S. Patent No. 4,976,953, to Orr et al., issued December 11, 1990.

iv. Hydrocarbons

[0055] Suitable hydrocarbons are straight and branched chain hydrocarbons having anywhere from 7 to 40 carbon atoms. Nonlimiting examples include mineral oil, petrolatum, squalene, isoparaffins, dodecane, isododecane, cholesterol, hydrogenated polyisobutylene, docosane (i.e. a C₂₂ hydrocarbon), hexadecane, isohexadecane (a commercially available hydrocarbon sold as Permethyl® 101A by Presperse, South Plainfield, NJ).

[0056] Mineral oil, which is also known as petrolatum liquid, is a mixture of liquid hydrocarbons obtained from petroleum. See The Merck Index, Tenth Edition, Entry 7048, p. 1033 (1983) and International Cosmetic Ingredient Dictionary, Fifth Edition, vol. 1, p.415-417 (1993).

[0057] Petrolatum, which is also known as petroleum jelly, is a colloidal system of nonstraight-chain solid hydrocarbons and high-boiling liquid hydrocarbons, in which most of the liquid hydrocarbons are held inside the micelles. See The Merck Index, Tenth Edition, Entry 7047, p. 1033 (1983); Schindler, Drug. Cosmet. Ind., 89, 36-37, 76, 78-80, 82 (1961); and International Cosmetic Ingredient Dictionary, Fifth Edition, vol. 1, p. 537 (1993).

40 v. Silicones

[0058] Nonvolatile silicones such as polydialkylsiloxanes, polydiarylsiloxanes, and polyalkaryl siloxanes are also useful herein. These silicones are disclosed in U.S. Patent No. 5,069,897, to Orr, issued December 3, 1991, which is incorporated by reference herein in its entirety. The polyalkylsiloxanes correspond to the general chemical formula R₃SiO[R₂SiO]_xSiR₃ wherein R is an alkyl group (preferably R is methyl or ethyl, more preferably methyl) and x is an integer up to about 500, chosen to achieve the desired molecular weight. Commercially available polyalkylsiloxanes include the polydimethylsiloxanes, which are also known as dimethicones, nonlimiting examples of which include the Vicasil® series sold by General Electric Company and the Dow Corning® 200 series sold by Dow Coming Corporation.

50 Specific examples of polydimethylsiloxanes useful herein include Dow Corning® 225 fluid having a viscosity of 10 centistokes and a boiling point greater than 200°C, and Dow Corning® 200 fluids having viscosities of 50, 350, and 12,500 centistokes, respectively, and boiling points greater than 200°C. Also useful are materials such as trimethylsiloxysilicate, which is a polymeric material corresponding to the general chemical formula [(CH₃)₃SiO_{1/2}x][SiO₂]y, wherein x is an integer from about 1 to about 500 and y is an integer from about 1 to about 500. A commercially available trimethylsiloxysilicate is sold as a mixture with dimethicone as Dow Corning® 593 fluid. Also useful herein are dimethiconols, which are hydroxy terminated dimethyl silicones. These materials can be represented by the general chemical formulas R₃SiO[R₂SiO]_xSiR₂OH and HOR₂SiO[R₂SiO]_xSiR₂OH wherein R is an alkyl group (preferably R is methyl or ethyl, more preferably methyl) and x is an integer up to about 500, chosen to achieve the desired molecular weight.

Commercially available dimethiconols are typically sold as mixtures with dimethicone or cyclomethicone (e.g. Dow Corning® 1401, 1402, and 1403 fluids). Also useful herein are polyalkylaryl siloxanes, with polymethylphenyl siloxanes having viscosities from about 15 to about 65 centistokes at 25°C being preferred. These materials are available, for example, as SF 1075 methylphenyl fluid (sold by General Electric Company) and 556 Cosmetic Grade phenyl trimethicone fluid (sold by Dow Coming Corporation).

5 vi. Waxes

10 [0059] Waxes which are potentially useful as the vehicle in the compositions herein include those set forth in CTFA Cosmetic Ingredient Handbook, Second Edition, 1992, pp. 535, which is herein incorporated by reference. Specific examples include beeswax, carnauba, candelilla wax, jojoba wax, lanolin wax, ozokerite, paraffin wax, and mixtures thereof.

15 vii. Triglycerides

[0060] Animal fats, vegetable oils and hydrogenated vegetable oils, and vegetable oil adducts are also potentially useful herein.
 20 [0061] Examples of vegetable oils and hydrogenated vegetable oils include safflower oil, castor oil, coconut oil, cottonseed oil, menhaden oil, palm kernel oil, palm oil, peanut oil, soybean oil, rapeseed oil, linseed oil, rice bran oil, pine oil, sesame oil, sunflower seed oil, hydrogenated safflower oil, hydrogenated castor oil, hydrogenated coconut oil, hydrogenated cottonseed oil, hydrogenated menhaden oil, hydrogenated palm kernel oil, hydrogenated palm oil, hydrogenated peanut oil, hydrogenated soybean oil, hydrogenated rapeseed oil, hydrogenated linseed oil, hydrogenated rice bran oil, hydrogenated sesame oil, hydrogenated sunflower seed oil, and mixtures thereof.

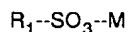
25 c. Surfactants

[0062] Surfactants can be desirably utilized as the vehicle in the compositions herein. Surfactants, if used, are typically employed at levels ranging from about 0.1% to about 30%, preferably from about 1% to about 15%, more preferably from about 0.1% to about 10% by weight of the composition. Suitable surfactants for use herein include cationic, nonionic, anionic, amphoteric and combinations thereof.

[0063] Nonlimiting examples of anionic Surfactants useful in the compositions of the present invention are disclosed in McCutcheon's, Detergents and Emulsifiers, North American edition (1986), published by allured Publishing Corporation; McCutcheon's, Functional Materials, North American Edition (1992); and U.S. Patent No. 3,929,678, to Laughlin et al., issued December 30, 1975.

[0064] A wide variety of anionic surfactants are useful herein. Nonlimiting examples of anionic surfactants include those selected from the group consisting of sarcosinates, sulfates, isethionates, taurates, phosphates, and mixtures thereof. Amongst the isethionates, the alkoyl isethionates are preferred, and amongst the sulfates, the alkyl and alkyl ether sulfates are preferred. The alkoyl isethionates typically have the formula $\text{RCO}-\text{OCH}_2\text{CH}_2\text{SO}_3\text{M}$ wherein R is alkyl or alkenyl of from about 10 to about 30 carbon atoms, and M is a water-soluble cation such as ammonium, sodium, potassium and triethanolamine. Nonlimiting examples of these isethionates include those alkoyl isethionates selected from the group consisting of ammonium cocoyl isethionate, sodium cocoyl isethionate, sodium lauroyl isethionate, and mixtures thereof.

[0065] The alkyl and alkyl ether sulfates typically have the respective formulae ROSO_3M and $\text{RO}(\text{C}_2\text{H}_4\text{O})_x\text{SO}_3\text{M}$, wherein R is alkyl or alkenyl of from about 10 to about 30 carbon atoms, x is from about 1 to about 10, and M is a water-soluble cation such as ammonium, sodium, potassium and triethanolamine. Another suitable class of anionic surfactants are the water-soluble salts of the organic, sulfuric acid reaction products of the general formula:



50 wherein R_1 is chosen from the group consisting of a straight or branched chain, saturated aliphatic hydrocarbon radical having from about 8 to about 24, preferably about 10 to about 16, carbon atoms; and M is a cation. Still other anionic synthetic surfactants include the class designated as succinamates, olefin sulfonates having about 12 to about 24 carbon atoms, and b-alkyloxy alkane sulfonates. Examples of these materials are sodium lauryl sulfate and ammonium lauryl sulfate.

[0066] Other anionic materials include the sarcosinates, nonlimiting examples of which include sodium lauroyl sarcosinate, sodium cocoyl sarcosinate, and ammonium lauroyl sarcosinate.

[0067] Other anionic materials useful herein are soaps (i.e. alkali metal salts, e.g., sodium or potassium salts) of

fatty acids, typically having from about 8 to about 24 carbon atoms, preferably from about 10 to about 20 carbon atoms. The fatty acids used in making the soaps can be obtained from natural sources such as, for instance, plant or animal-derived glycerides (e.g., palm oil, coconut oil, soybean oil, castor oil, tallow, lard, etc.) The fatty acids can also be synthetically prepared. Soaps are described in more detail in U.S. Patent No. 4,557,853, cited above.

5 [0068] Other anionic materials include phosphates such as monoalkyl, dialkyl, and trialkylphosphate salts.

[0069] Other anionic materials include alkanoyl sarcosinates corresponding to the formula RCON(CH₃)CH₂CH₂CO₂M wherein R is alkyl or alkenyl of about 10 to about 20 carbon atoms, and M is a water-soluble cation such as ammonium, sodium, potassium and trialkanolamine (e.g., triethanolamine), a preferred example of which is sodium lauroyl sarcosinate.

10 [0070] Also useful are taurates which are based on taurine, which is also known as 2-aminoethanesulfonic acid. Examples of taurates include N-alkyltaurines such as the one prepared by reacting dodecylamine with sodium isethionate according to the teaching of U.S. Patent 2,658,072 which is incorporated herein by reference in its entirety.

[0071] Nonlimiting examples of preferred anionic surfactants useful herein include those selected from the group consisting of sodium lauryl sulfate, ammonium lauryl sulfate, ammonium laureth sulfate, sodium laureth sulfate, sodium trideceth sulfate, ammonium cetyl sulfate, sodium cetyl sulfate, ammonium cocoyl isethionate, sodium lauroyl isethionate, sodium lauroyl sarcosinate, and mixtures thereof.

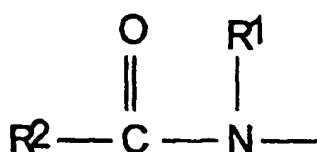
15 [0072] Nonlimiting examples of nonionic surfactants for use in the compositions of the present invention are disclosed in McCutcheon's, Detergents and Emulsifiers, North American edition (1986), published by allured Publishing Corporation; and McCutcheon's, Functional Materials, North American Edition (1992);

20 [0073] Nonionic surfactants useful herein include those selected from the group consisting of alkyl glucosides, alkyl polyglucosides, polyhydroxy fatty acid amides, alkoxylated fatty acid esters, sucrose esters, amine oxides, and mixtures thereof.

[0074] Alkyl glucosides and alkyl polyglucosides are useful herein, and can be broadly defined as condensation products of long chain alcohols, e.g. C₈-30 alcohols, with sugars or starches or sugar or starch polymers, i.e., glycosides or polyglycosides. These compounds can be represented by the formula (S)_n-O-R wherein S is a sugar moiety such as glucose, fructose, mannose, and galactose; n is an integer of from about 1 to about 1000, and R is a C₈-30 alkyl group. Examples of long chain alcohols from which the alkyl group can be derived include decyl alcohol, cetyl alcohol, stearyl alcohol, lauryl alcohol, myristyl alcohol, oleyl alcohol, and the like. Preferred examples of these surfactants include those wherein S is a glucose moiety, R is a C₈-20 alkyl group, and n is an integer of from about 1 to about 9.

25 [0075] Commercially available examples of these surfactants include decyl polyglucoside (available as APG 325 CS from Henkel) and lauryl polyglucoside (available as APG 600CS and 625 CS from Henkel). Also useful are sucrose ester surfactants such as sucrose cocoate and sucrose laurate.

30 [0076] Other useful nonionic surfactants include polyhydroxy fatty acid amide surfactants, more specific examples of which include glucosamides, corresponding to the structural formula:



40 wherein: R¹ is H, C₁-C₄ alkyl, 2-hydroxyethyl, 2-hydroxy- propyl, preferably C₁-C₄ alkyl, more preferably methyl or ethyl, most preferably methyl; R² is C₅-C₃₁ alkyl or alkenyl, preferably C₇-C₁₉ alkyl or alkenyl, more preferably C₉-C₁₇ alkyl or alkenyl, most preferably C₁₁-C₁₅ alkyl or alkenyl. An especially preferred surfactant corresponding to the above structure is coconut alkyl N-methyl glucoside amide (i.e., wherein the R²CO- moiety is derived from coconut oil fatty acids). Processes for making compositions containing polyhydroxy fatty acid amides are disclosed, for example, in G. B. Patent Specification 809,060, published February 18, 1959, by Thomas Hedley & Co., Ltd.; U.S. Patent No. 2,965,576, to E.R. Wilson, issued December 20, 1960; U.S. Patent No. 2,703,798, to A.M. Schwartz, issued March 8, 1955; and U.S. Patent No. 1,985,424, to Piggott, issued December 25, 1934.

45 [0076] Other examples of nonionic surfactants include amine oxides. Amine oxides correspond to the general formula R₁R₂R₃NO, wherein R₁ contains an alkyl, alkenyl or monohydroxy alkyl radical of from about 8 to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties, and from 0 to about 1 glyceryl moiety, and R₂ and R₃ contain from about 1 to about 3 carbon atoms and from 0 to about 1 hydroxy group, e.g., methyl, ethyl, propyl, hydroxyethyl, or hydroxypropyl radicals. The arrow in the formula is a conventional representation of a semipolar bond. Examples of amine oxides suitable for use in this invention include dimethyl-dodecylamine oxide, oleyldi(2-hydroxyethyl) amine oxide, dimethyloctylamine oxide, dimethyl-decyldamine oxide, dimethyl-tetradecylamine oxide, 3,6,9-trioxaheptade-

cyldiethylamine oxide, di(2-hydroxyethyl)-tetradecylamine oxide, 2-dodecoxyethyldimethylamine oxide, 3-dodecoxy-2-hydroxypropyldi(3-hydroxypropyl)amine oxide, dimethylhexadecylamine oxide.

[0077] The term "amphoteric surfactant," as used herein, is also intended to encompass zwitterionic surfactants, which are well known to formulators skilled in the art as a subset of amphoteric surfactants.

5 [0078] A wide variety of amphoteric surfactants can be used in the compositions of the present invention. Particularly useful are those which are broadly described as derivatives of aliphatic secondary and tertiary amines, preferably wherein the nitrogen is in a cationic state, in which the aliphatic radicals can be straight or branched chain and wherein one of the radicals contains an ionizable water solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate.

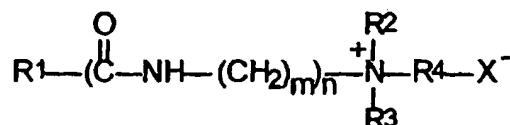
10 [0079] Nonlimiting examples of amphoteric surfactants useful in the compositions of the present invention are disclosed in McCutcheon's, Detergents and Emulsifiers, North American edition (1986), published by allured Publishing Corporation; and McCutcheon's, Functional Materials, North American Edition (1992).

15 [0080] Nonlimiting examples of amphoteric or zwitterionic surfactants are those selected from the group consisting of betaines, sultaines, hydroxysultaines, alkyliminoacetates, iminodialkanoates, aminoalkanoates, and mixtures thereof.

20 [0081] Examples of betaines include the higher alkyl betaines, such as coco dimethyl carboxymethyl betaine, lauryl dimethyl carboxymethyl betaine, lauryl dimethyl alphacarboxyethyl betaine, cetyl dimethyl carboxymethyl betaine, cetyl dimethyl betaine (available as Lonzaine 16SP from Lonza Corp.), lauryl bis-(2-hydroxyethyl) carboxymethyl betaine, oleyl dimethyl gamma-carboxypropyl betaine, lauryl bis-(2-hydroxypropyl)alpha-carboxyethyl betaine, coco dimethyl sulfopropyl betaine, lauryl dimethyl sulfoethyl betaine, lauryl bis-(2-hydroxyethyl) sulfopropyl betaine, amidobetaines and amidosulfobetaines (wherein the RCONH(CH₂)₃ radical is attached to the nitrogen atom of the betaine), oleyl betaine (available as amphoteric Velvetex OLB-50 from Henkel), and cocamidopropyl betaine (available as Velvetex BK-35 and BA-35 from Henkel).

25 [0082] Examples of sultaines and hydroxysultaines include materials such as cocamidopropyl hydroxysultaine (available as Mirataine CBS from Rhone-Poulenc).

[0083] Preferred for use herein are amphoteric surfactants having the following structure:

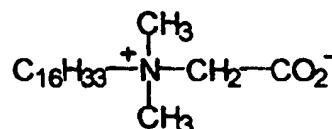


35 wherein R¹ is unsubstituted, saturated or unsaturated, straight or branched chain alkyl having from about 9 to about 22 carbon atoms. Preferred R¹ has from about 11 to about 18 carbon atoms; more preferably from about 12 to about 18 carbon atoms; more preferably still from about 14 to about 18 carbon atoms; m is an integer from 1 to about 3, more preferably from about 2 to about 3, and more preferably about 3; n is either 0 or 1, preferably 1; R² and R³ are independently selected from the group consisting of alkyl having from 1 to about 3 carbon atoms, unsubstituted or mono-substituted with hydroxy, preferred R² and R³ are CH₃; X is selected from the group consisting of CO₂, SO₃ and SO₄; R⁴ is selected from the group consisting of saturated or unsaturated, straight or branched chain alkyl, unsubstituted or monosubstituted with hydroxy, having from 1 to about 5 carbon atoms. When X is CO₂, R⁴ preferably has 1 or 3 carbon atoms, more preferably 1 carbon atom. When X is SO₃ or SO₄, R⁴ preferably has from about 2 to about 4 carbon atoms, more preferably 3 carbon atoms.

45 [0084] Examples of amphoteric surfactants of the present invention include the following compounds:

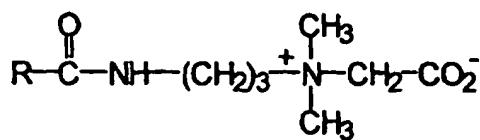
Cetyl dimethyl betaine (this material also has the CTFA designation cetyl betaine)

50

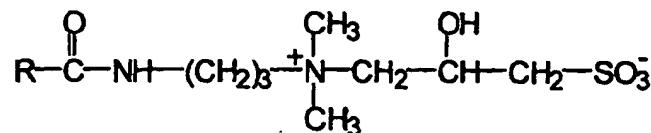


55

Cocamidopropylbetaine



10 wherein R has from about 9 to about 13 carbon atoms
Cocamidopropyl hydroxy sultaine

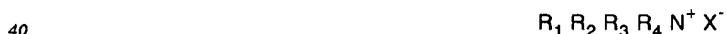


20 wherein R has from about 9 to about 13 carbon atoms,

[0085] Examples of other useful amphoteric surfactants are alkyliminoacetates, and iminodialkanoates and aminoalkanoates of the formulas $\text{RN}(\text{CH}_2)_m\text{CO}_2\text{M}_2$ and $\text{RNH}(\text{CH}_2)_m\text{CO}_2\text{M}$ wherein m is from 1 to 4, R is a C₈-C₂₂ alkyl or alkenyl, and M is H, alkali metal, alkaline earth metal ammonium, or alkanolammonium. Also included are imidazolinium and ammonium derivatives. Specific examples of suitable amphoteric surfactants include sodium 3-dodecyl-amino-propionate, sodium 3-dodecylaminopropane sulfonate, N-higher alkyl aspartic acids such as those produced according to the teaching of U.S. Patent 2,438,091 which is incorporated herein by reference in its entirety; and the products sold under the trade name "Miranol" and described in U.S. Patent 2,528,378. Other examples of useful amphotetics include 30 amphoteric phosphates, such as coamidopropyl PG-dimonium chloride phosphate (commercially available as Mon aquat PTC, from Mona Corp.). Also useful are amphoacetates such as disodium lauroamphodiacetate, sodium lauroamphoacetate, and mixtures thereof.

[0086] Nonlimiting examples of cationic surfactants useful herein are disclosed in McCutcheon's, Detergents and Emulsifiers, North American edition (1986), published by allured Publishing Corporation; and McCutcheon's, Functional Materials, North American Edition (1992).

[0087] Nonlimiting examples of cationic surfactants useful herein include cationic alkyl ammonium salts such as those having the formula:



wherein R₁ is selected from an alkyl group having from about 12 to about 18 carbon atoms, or aromatic, aryl or alkaryl groups having from about 12 to about 18 carbon atoms; R₂, R₃, and R₄ are independently selected from hydrogen, an alkyl group having from about 1 to about 18 carbon atoms, or aromatic, aryl or alkaryl groups having from about 12 to about 18 carbon atoms; and X is an anion selected from chloride, bromide, iodide, acetate, phosphate, nitrate, sulfate, methyl sulfate, ethyl sulfate, tosylate, lactate, citrate, glycolate, and mixtures thereof. Additionally, the alkyl groups can also contain ether linkages, or hydroxy or amino group substituents (e.g., the alkyl groups can contain polyethylene glycol and polypropylene glycol moieties).

[0088] More preferably, R₁ is an alkyl group having from about 12 to about 18 carbon atoms; R₂ is selected from H or an alkyl group having from about 1 to about 18 carbon atoms; R₃ and R₄ are independently selected from H or an alkyl group having from about 1 to about 3 carbon atoms; and X is as described in the previous paragraph.

[0089] Most preferably, R₁ is an alkyl group having from about 12 to about 18 carbon atoms; R₂, R₃, and R₄ are selected from H or an alkyl group having from about 1 to about 3 carbon atoms; and X is as described previously.

[0090] Alternatively, other useful cationic surfactants include amino-amides, wherein in the above structure R₁ is alternatively R₅CO-(CH₂)_n-, wherein R₅ is an alkyl group having from about 12 to about 22 carbon atoms, and n is an integer from about 2 to about 6, more preferably from about 2 to about 4, and most preferably from about 2 to about 3. Nonlimiting examples of these cationic emulsifiers include stearamidopropyl PG-dimonium chloride phosphate, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate) ammonium chloride, stear-

amidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof.

[0091] Nonlimiting examples of quaternary ammonium salt cationic surfactants include those selected from the group consisting of cetyl ammonium chloride, cetyl ammonium bromide, lauryl ammonium chloride, lauryl ammonium bromide, stearyl ammonium chloride, stearyl ammonium bromide, cetyl dimethyl ammonium chloride, cetyl dimethyl ammonium bromide, lauryl dimethyl ammonium chloride, lauryl dimethyl ammonium bromide, stearyl dimethyl ammonium chloride, stearyl dimethyl ammonium bromide, cetyl trimethyl ammonium chloride, cetyl trimethyl ammonium bromide, lauryl trimethyl ammonium chloride, lauryl trimethyl ammonium bromide, stearyl trimethyl ammonium chloride, stearyl trimethyl ammonium bromide, lauryl dimethyl ammonium chloride, stearyl dimethyl cetyl ditallow dimethyl ammonium chloride, dicetyl ammonium chloride, dicetyl ammonium bromide, dilauryl ammonium chloride, dilauryl ammonium bromide, distearyl ammonium chloride, distearyl ammonium bromide, dicetyl methyl ammonium chloride, dicetyl methyl ammonium bromide, dilauryl methyl ammonium chloride, dilauryl methyl ammonium bromide, distearyl methyl ammonium chloride, distearyl dimethyl ammonium chloride, distearyl methyl ammonium bromide, and mixtures thereof. Additional quaternary ammonium salts include those wherein the C12 to C22 alkyl carbon chain is derived from a tallow fatty acid or from a coconut fatty acid. The term "tallow" refers to an alkyl group derived from tallow fatty acids (usually hydrogenated tallow fatty acids), which generally have mixtures of alkyl chains in the C16 to C18 range. The term "coconut" refers to an alkyl group derived from a coconut fatty acid, which generally have mixtures of alkyl chains in the C12 to C14 range. Examples of quaternary ammonium salts derived from these tallow and coconut sources include ditallow dimethyl ammonium chloride, ditallow dimethyl ammonium methyl sulfate, di(hydrogenated tallow) dimethyl ammonium chloride, di(hydrogenated tallow) dimethyl ammonium acetate, ditallow dipropyl ammonium phosphate, ditallow dimethyl ammonium nitrate, di(coconutalkyl)dimethyl ammonium chloride, di(coconutalkyl)dimethyl ammonium bromide, tallow ammonium chloride, coconut ammonium chloride, stearamidopropyl PG-dimonium chloride phosphate, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate) ammonium chloride, stearamidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof.

[0092] Preferred cationic surfactants useful herein include those selected from the group consisting of dilauryl dimethyl ammonium chloride, distearyl dimethyl ammonium chloride, dimyristyl dimethyl ammonium chloride, dipalmityl dimethyl ammonium chloride, distearyl dimethyl ammonium chloride, and mixtures thereof.

30 d. Thickeners/Binders

[0093] Another category of functional ingredients which can be employed in the compositions used in the method of the present invention are thickeners and binders. A thickener or binder will usually be present in amounts anywhere from 0.01% to 20% by weight, preferably from about 0.1% to about 10%, more preferably from about 0.1% to about 5% by weight of the composition. Suitable thickeners include cross-linked polyacrylate materials available under the trademark Carbopol from the B. F. Goodrich Company. Gums may be employed such as xanthan, carrageenan, gelatin, karaya, pectin and locust bean gum. Under certain circumstances the thickening function may be accomplished by a material also serving as a silicone or emollient. For instance, silicone gums in excess of 10 centistokes and esters such as glycerol stearate have dual functionality.

[0094] Preferred binders include, but are not limited to methycellulose, sodium carboxymethycellulose, hydroxypropylmethylcellulose, carbomer, polyvinylpyrrolidone, acacia, guar gum, xanthan gum and tragacanth. Particularly preferred are methycellulose, carbomer, xanthan gum, guar gum, polyvinylpyrrolidone and sodium carboxymethycellulose

45 e. Flavoring Agents

[0095] Flavoring agents among those useful herein include those described in *Remington's Pharmaceutical Sciences*, 18th Edition, Mack Publishing Company, 1990, pp. 1288-1300, incorporated by reference herein. Dyes, or pigments among those useful herein include those described in *Handbook of Pharmaceutical Excipients*, Second Edition pp. 126-134, 1994 by the American Pharmaceutical Association & the Pharmaceutical Press, incorporated by reference herein.

50 f. Buffering Systems

[0096] Preferred buffer systems include, but are not limited to potassium acetate, boric carbonic, phosphoric, succinic, malic, tartaric, citric, acetic, benzoic, lactic, glyceric, gluconic, glutaric and glutamic. Particularly preferred are phosphoric, tartaric, citric, and potassium acetate.

g. Preservatives

[0097] Preferred preservatives include, but are not limited to, phenol, alkyl esters of parahydroxybenzoic acid, benzoic acid and the salts thereof, boric acid and the thereof, sorbic acid and the salts thereof, chorbutanol, benzyl alcohol, thimerosal, phenylmercuric acetate and nitrate, nitromersol, benzalkonium chloride, cetylpyridinium chloride, methyl paraben, and propyl paraben. Particularly preferred are the salts of benzoic acid, benzalkonium chloride, methyl paraben and propyl paraben.

h. Sweeteners

[0098] Preferred sweeteners include, but are not limited to, sucrose, glucose, saccharin, and aspartame. Particularly preferred are sucrose and saccharin.

i. Fillers

[0099] Preferred fillers include, but are not limited to lactose, sucrose, maltodextrin, mannitol, starch 1500, dicalcium phosphate and microcrystalline cellulose.

j. Plasticizers

[0100] Preferred plasticizers include, but are not limited to polyethylene glycol, propylene glycol, dibutyl phthalate, and castor oil, acetylated monoglycerides, and triacetin.

k. Lubricants

[0101] Preferred lubricants include, but are not limited to, magnesium stearate, stearic acid, and talc.

l. Disintegrants

[0102] Preferred disintegrants include, but are not limited to, crospovidone, sodium carboxymethyl starch, sodium starch glycolate, sodium carboxymethyl cellulose, alginic acid, clays, and ion exchange resins.

m. Polymers

[0103] Preferred polymers, include but are not limited to hydroxypropylmethylcellulose (HPMC) alone and/ or in combination with hydroxypropylcellulose (HPC), carboxymethylcellulose, acrylic resins such as Eudragit® RL30D, manufactured by Rohm Pharma GmbH Weiderstadt, West Germany, methylcellulose, ethylcellulose, and polyvinylpyrrolidone or other commercially available film-coating preparations such as Dri-Klear, manufactured by Crompton & Knowles Corp., Mahwah, NJ or Opadry manufactured by Colorcon, West Point, PA.

2. Other Hair Growth Agents

[0104] The compositions herein may also optionally comprise an activity enhancer or enhancers. The activity enhancer or enhancers can be chosen from a wide variety of molecules which can function in different ways to enhance the hair growth effects of a compound of the present invention. These optional activity enhancers, when present, are typically employed in the compositions herein at a level ranging from about 0.01% to about 15%, preferably from about 0.1% to about 10%, most preferably from about 0.5% to about 5% by weight of the composition.

[0105] Vasodilators such as potassium channel agonists including, for example, minoxidil and minoxidil derivatives such as aminexil and such as those described in U.S. Patent 3,382,247, U.S. Patent 5,756,092, issued May 26, 1998, U.S. Patent 5,772,990, issued June 30, 1998, U.S. Patent 5,760,043, issued June 2, 1998, U.S. Patent 328,914, issued July 12, 1994, U.S. Patent 5,466,694, issued November 14, 1995, 5,438,058, issued August 1, 1995, and U.S. Patent 4,973,474, issued November 27, 1990, (all of which are herein incorporated by reference), and cromakalim and diazoxide can be used as optional activity enhancers in the compositions herein.

[0106] One suitable class of optional activity enhancer for use herein are antiandrogens. Examples of suitable antiandrogens may include, but are not limited 5- α -reductase inhibitors such as finesteride and those described in U.S. Patent 5,516,779, issued May 14, 1996 (herein incorporated by reference) and in Nnane et al, *Cancer Research* 58, "Effects of Some Novel Inhibitors of C17,20-Lyase and 5 α -Reductase *in Vitro* and *in Vivo* and Their Potential Role in the Treatment of Prostate Cancer., as well as cyproterone acetate, azelaic acid and its derivatives and those compounds

described in U.S. Patent 5,480,913, issued January 2, 1996, flutamide, and those described in U.S. Patents 5,411,981, issued May 2, 1995, U.S. Patent 5,565,467, issued October 15, 1996 and U.S. Patent 4,910,226, issued March 20, 1990.

[0107] Another suitable class of optional activity enhancers are immunosuppressants such as 1) cyclosporin and cyclosporin analogs including those described in U.S. Provisional Patent Application No. 60/122,925, Fulmer et al., "Method of Treating Hair Loss Using Non-Immunosuppressive Compounds", filed March 5, 1999, herein incorporated by reference, and 2) FK506 analogs such as those described in U.S. Provisional Patent Application No. 60/102,449, McIver et al., "Heterocyclic 2-Substituted Ketoamides", filed September 30, 1998, U.S. Provisional Patent Application No. 60/102,448, McIver et al., "2-Substituted Ketoamides", filed September 30, 1998, U.S. Provisional Patent Application No. 60/102,539, McIver et al., "2-Substituted Heterocyclic Sulfonamides", filed September 30, 1998, U.S. Provisional Patent Application No. 60/102,458, Tiesman et al., "Method of Treating Hair Loss Using Ketoamides", filed September 30, 1998, and U.S. Provisional Patent Application No. 60/102,437, McIver et al., "Method of Treating Hair Loss Using Sulfonamides", filed September 30, 1998.

[0108] Another suitable class of optional activity enhancers are antimicrobials such as selenium sulfide, ketoconazole, triclocarbon, triclosan, zinc pyrithione, itraconazole, asiatic acid, hinokitiol, miprocin and those described in EPA 0,680,745, clinacycin hydrochloride, benzoyl peroxide, benzyl peroxide and minocycline.

[0109] Anti-inflammatories can also be incorporated into the compositions herein as an optional activity enhancer. Examples of suitable anti-inflammatories may include glucocorticoids such as hydrocortisone, mometasone furate and prednisolone, nonsteroidal anti-inflammatories including cyclooxygenase or lipoxygenase inhibitors such as those described in U.S. Patent 5,756,092, and benzydamine, salicylic acid, and those compounds described in EPA 0,770,399, published May 2, 1997, WO 94/06434, published March 31, 1994 and FR 2,268,523, published November 21, 1975.

[0110] Another suitable class of optional activity enhancers are thyroid hormones and derivatives and analogs thereof. Examples of suitable thyroid hormones for use herein may include triiodothyronine. Examples of thyroid hormone analogs which may be suitable for use herein include those described in U.S. Provisional Patent Application No.

25 60/136,996, Zhang et al., "Method of Treating Hair Loss", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,024, Zhang et al., "Method of Treating Hair Loss Using Biphenyl Compounds", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,022, Zhang et al., "Method of Treating Hair Loss Using Carboxyl Derivatives", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,023, Zhang et al., "Method of Treating Hair Loss Using Sulfonyl Thyromimetic Compounds", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,052, Youngquist et al., "Biaryl Compounds", filed June 1, 1999, U.S. Provisional Patent Application No. 60/137,063, Youngquist et al., "Sulfur-Bridged Compounds", filed June 1, 1999, and U.S. Provisional Patent Application No. 60/136,958, Youngquist et al., "Substituted Biaryl Ether Compounds", filed June 1, 1999.

[0111] Prostaglandin agonists or antagonists can also be used as optional activity enhancers in the compositions herein. Examples of suitable prostaglandins agonists or antagonists include latanoprost and those described in WO 98/33497, Johnstone, published August 6, 1998, WO 95/11003, Stjernschantz, published April 27, 1995, JP 97-100091, and Ueno, JP 96-134242, Nakamura.

[0112] Another class of optional activity enhancers for use herein are retinoids. Suitable retinoids may include isotretinoin, acitretin, tazarotene,

[0113] Non-limiting examples of penetration enhancers which may be used as optional activity enhancers herein include, for example, 2-methyl propan-2-ol, propan-2-ol, ethyl-2-hydroxypropanoate, hexan-2,5-diol, POE(2) ethyl ether, di(2-hydroxypropyl) ether, pentan-2,4-diol, acetone, POE(2) methyl ether, 2-hydroxypropionic acid, 2-hydroxyoctanoic acid, progan-1-ol, 1,4-dioxane, tetrahydrofuran, butan-1,4-diol, propylene glycol dipelargonate, polyoxypropylene 15 stearyl ether, octyl alcohol, POE ester of oleyl alcohol, oleyl alcohol, lauryl alcohol, dioctyl adipate, dicapryl adipate, di-isopropyl adipate, di-isopropyl sebacate, dibutyl sebacate, diethyl sebacate, dimethyl sebacate, diethyl sebacate, dibutyl sebacate, diethyl azelate, dibenzyl sebacate, dibutyl phthalate, dibutyl azelate, ethyl myristate, dimethyl azelate, butyl myristate, dibutyl succinate, didecyl phthalate, decyl oleate, ethyl caproate, ethyl salicylate, iso-propyl palmitate, ethyl laurate, 2-ethyl-hexyl pelargonate, iso-propyl isostearate, butyl laurate, benzyl benzoate, butyl benzoate, hexyl laurate, ethyl caprate, ethyl caprylate, butyl stearate, benzyl salicylate, 2-hydroxypropanoic acid, 2-hydroxyoctanoic acid, methylsulfoxide, N,N-dimethyl acetamide, N,N-dimethyl formamide, 2-pyrrolidone, 1-methyl-2-pyrrolidone, 5-methyl-2-pyrrolidone, 1,5-dimethyl-2-pyrrolidone, 1-ethyl-2-pyrrolidone, phosphine oxides, sugar esters, tetrahydrofurfural alcohol, urea, diethyl-*m*-toluamide, 1-dodecylazacycloheptan-2-one and those described in U.S. Patent 5,015,470, issued May 14, 1991 and U.S. Patent 5,496,827, issued July 15, 1994.

[0114] Other classes of optional activity enhancers for use herein include flavinoids, ascomycin derivatives and analogs, histamine antagonists such as diphenhydramine hydrochloride, other triterpenes such as oleanolic acid and ursolic acid and those described in U.S. Patent 5,529,769, JP 10017431, WO 95/35103, U.S. Patent 5,468,888, JP 09067253, WO 92/09262, JP 62093215, U.S. Patent 5,631,282, U.S. Patent 5,679,705, JP 08193094, JP 07010722, JP 60126218, JP 07133288, JP 10265328 saponins such as those described in EP 0,558,509 to Bonte et al, published September 8, 1993 and WO 97/01346 to Bonte et al, published January 16, 1997, proeoglycanase or glycosaminogly-

canase inhibitors such as those described in U.S. Patents 5,015,470, issued May 14, 1991, U.S. Patent 5,300,284, issued April 5, 1994 and U.S. Patent 5,185,325, issued February 9, 1993 estrogen agonists and antagonists, pseudo-
5 terins, cytokine and growth factor promotores, analogs or inhibitors such as interleukin 1 inhibitors, interleukin-6 inhibitors, interleukin-10 promotores, and tumor necrosis factor inhibitors, vitamins such as vitamin D analogs and parathyroid hormone antagonists, Vitamin B12 analogs and panthenol, interfuron agonists and antagonists, hydroxyacids such as those described in U.S. Patent 5,550,158, benzophenones and hydantoin anticonvulsants such as phenytoin.

[0115] Other hair growth agents are described in detail in, for example, JP 09-157,139 to Tsuji et al, published June 17, 1997; EP 0277455 A1 to Mirabeau, published August 10, 1988; WO 97/05887 to Cabo Soler et al, published February 20, 1997; WO 92/16186 to Bonte et al, published March 13, 1992; JP 62-93215 to Okazaki et al, published 10 April 28, 1987; U.S. Patent 4,987,150 to Kurono et al, issued January 22, 1991; JP 290811 to Ohba et al, published October 15, 1992; JP 05-286,835 to Tanaka et al, published November 2, 1993, FR 2,723,313 to Greff, published August 2, 1994, U. S. Patent 5,015,470 to Gibson, issued May 14, 1991, U.S. Patent 5,559,092, issued September 24, 1996, U.S. patent 5,536,751, issued July 16, 1996, U.S. Patent 5,714,515, issued February 3, 1998, EPA 0,319,991, published June 14, 1989, EPA 0,357,630, published October 6, 1988, EPA 0,573,253, published December 8, 1993, 15 JP 61-260010, published November 18, 1986, U.S. Patent 5,772,990, issued June 30, 1998, U.S. Patent 5,053,410, issued October 1, 1991, and U.S. Patent 4,761,401, issued August 2, 1988.

3. Other Active Ingredients

[0116] In addition to other hair growth agents, other hair or skin active agents can be incorporated into the compositions herein in safe and effective amounts.

[0117] The term "safe and effective amount" as used herein, means an amount of an active ingredient high enough to modify the condition to be treated or to deliver the desired skin or hair benefit, but low enough to avoid serious side effects, at a reasonable benefit to risk ratio within the scope of sound medical judgment. What is a safe and effective amount of the active ingredient will vary with the specific active, the ability of the active to penetrate through the skin/hair, the age, health condition, and skin/hair condition of the user, and other like factors.

[0118] The active ingredients useful herein can be categorized by their therapeutic benefit or their postulated mode of action. However, it is to be understood that the active ingredients useful herein can in some instances provide more than one therapeutic benefit or operate via more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit the active ingredient to that particular application or applications listed. Also, pharmaceutically-acceptable salts of these active ingredients are useful herein. The following active ingredients can potentially be useful in the compositions of the present invention.

Non-Steroidal Anti-Inflammatory Actives (NSAIDS): Examples of NSAIDS include the following categories: propionic acid derivatives; acetic acid derivatives; fenamic acid derivatives; biphenylcarboxylic acid derivatives; and oxicams. All of these NSAIDS are fully described in U.S. Patent 4,985,459 to Sunshine et al., issued January 15, 1991. Examples of useful NSAIDS include acetyl salicylic acid, ibuprofen, naproxen, benoxaprofen, flurbiprofen, fenoprofen, fenbufen, ketoprofen, indoprofen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, tiaprofenic acid, fluprofen and bucloxic acid. Also useful are the steroidal anti-inflammatory drugs including hydrocortisone and the like.

Topical Anesthetics: Examples of topical anesthetic drugs include benzocaine, lidocaine, bupivacaine, chlorprocaine, dibucaine, etidocaine, mepivacaine, tetracaine, dyclonine, hexylcaine, procaine, cocaine, ketamine, pramoxine, phenol, and pharmaceutically acceptable salts thereof.

Antimicrobial and Antifungal Actives: Examples of antimicrobial and antifungal actives include β -lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, 2,4,4'-trichloro-2'-hydroxy diphenyl ether, 3,4,4'-trichlorobanilide, phenoxyethanol, phenoxy propanol, phenoxyisopropanol, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, hexamidine isethionate, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin, miconazole, tetracycline hydrochloride, erythromycin, zinc erythromycin, erythromycin estolate, erythromycin stearate, amikacin sulfate, doxycycline hydrochloride, capreomycin sulfate, chlorhexidine gluconate, chlorhexidine hydrochloride, chlortetracycline hydrochloride, oxytetracycline hydrochloride, clindamycin hydrochloride, ethambutol hydrochloride, metronidazole hydrochloride, pentamidine hydrochloride, gentamicin sulfate, kanamycin sulfate, lineomycin hydrochloride, methacycline hydrochloride, methenamine hippurate, methenamine mandelate, minocycline hydrochloride, neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, octopirox, parachlorometaxylenol, nystatin, tolnaftate, zinc pyrithione and clotrimazole.

Sunscreen Actives: Also useful herein are sunscreening actives. A wide variety of sun screening agents are described in U.S. Patent No. 5,087,445, to Haffey et al., issued February 11, 1992; U.S. Patent No. 5,073,372, to Turner et al., issued December 17, 1991; U.S. Patent No. 5,073,371, to Turner et al. issued December 17, 1991; and Segarin, et

al., at Chapter VIII, pages 189 et seq., of *Cosmetics Science and Technology*. Nonlimiting examples of sunscreens which are useful in the compositions of the present invention are those selected from the group consisting of 2-ethylhexyl *p*-methoxycinnamate, 2-ethylhexyl N,N-dimethyl-*p*-aminobenzoate, *p*-aminobenzoic acid, 2-phenylbenzimidazole-5-sulfonic acid, octocrylene, oxybenzone, homomenthyl salicylate, octyl salicylate, 4,4'-methoxy-*t*-butyldibenzoylmethane, 4-isopropyl dibenzoylmethane, 3-benzylidene camphor, 3-(4-methylbenzylidene) camphor, titanium dioxide, zinc oxide, silica, iron oxide, and mixtures thereof. Still other useful sunscreens are those disclosed in U.S. Patent No. 4,937,370, to Sabatelli, issued June 26, 1990; and U.S. Patent No. 4,999,186, to Sabatelli et al., issued March 12, 1991. Especially preferred examples of these sunscreens include those selected from the group consisting of 4-N, N-(2-ethylhexyl)methylaminobenzoic acid ester of 2,4-dihydroxybenzophenone, 4-N,N-(2-ethylhexyl)methylaminobenzoic acid ester with 4-hydroxydibenzoylmethane, 4-N,N-(2-ethylhexyl)-methylaminobenzoic acid ester of 2-hydroxy-4-(2-hydroxyethoxy)benzophenone, 4-N,N-(2-ethylhexyl)-methylaminobenzoic acid ester of 4-(2-hydroxyethoxy)dibenzoylmethane, and mixtures thereof. Exact amounts of sunscreens which can be employed will vary depending upon the sunscreen chosen and the desired Sun Protection Factor (SPF) to be achieved. SPF is a commonly used measure of photoprotection of a sunscreen against erythema. See *Federal Register*, Vol. 43, No. 166, pp. 38206-38269, August 25, 1978.

4. Miscellaneous

[0119] The compositions of the present invention can comprise a wide range of other optional components. These additional components should be pharmaceutically acceptable. The *CTFA Cosmetic Ingredient Handbook*, Second Edition, 1992, which is incorporated by reference herein in its entirety, describes a wide variety of nonlimiting cosmetic and pharmaceutical ingredients commonly used in the skin care industry, which are suitable for use in the compositions of the present invention. Nonlimiting examples of functional classes of ingredients are described at page 537 of this reference. Examples of these and other functional classes include: abrasives, absorbents, anticaking agents, antioxidants, vitamins, biological additives, bulking agents, chelating agents, chemical additives, colorants, cosmetic astringents, cosmetic biocides, denaturants, drug astringents, external analgesics, film formers, fragrance components, opacifying agents, pH adjusters, propellants, reducing agents, and skin bleaching agents.

II. THE METHOD

[0120] The method of the present invention involves the administration of the compositions described herein for regulating hair growth in mammals (e.g., humans and domestic animals). In one embodiment, the present invention provides for the prevention of hair loss. In another embodiment, the present invention provides for the use of compositions containing betulinic acid for stimulating new hair growth.

[0121] The compositions of the present invention can be administered topically, orally or parenterally. The preferred method of the present invention involves the topical application of the compositions described herein to the scalp, particularly where the scalp is already bald or balding. The amount of the composition and the frequency of application to the hair and/or scalp/skin can vary widely, depending on the desired effect and/or personal needs. Typically the composition is applied from about 1 to about 10 times per day, more typically from about 1 to about 6 times per day and most typically from 1 to 3 times per day.

[0122] The topical compositions can be delivered the hair/scalp/skin from a variety of delivery devices. For example, the compositions can be incorporated into a medicated cleansing pad. Preferably these pads comprise form about 50% to about 75% of a substrate and from about 25% to about 50% of a liquid composition deliverable from the substrate. Suitable pads are described, for example, in U.S. Patent 4,891,228; Thurman et al.; issued January 2, 1990; and U.S. Patent 4,891,227; Thaman et al.; issued January 2, 1990.

[0123] Alternatively, the compositions useful herein can be incorporated into and delivered from a soft-tipped or flexible dispensing device. These devices are useful for the controlled delivery of the compositions to the skin surface and have the advantage that the treatment composition itself never need be directly handled by the user. Nonlimiting examples of these devices comprise a fluid container including a mouth, an applicator, means for holding the applicator

in the mouth of the container and a normally closed pressure-responsive valve for permitting the flow of fluid from the container to the applicator upon the application of pressure to the valve. The fluid preferably contains from about 0.01% to about 20% of betulinic acid, preferably from about 0.1% to about 10%, more preferably from about 1% to about 5%.

[0124] The valve can include a diaphragm formed from an elastically fluid impermeable material with a plurality of non-intersecting acruate slits therein, where each slit has a base which is intersected by at least one other slit, and where each slit is out of intersecting relation with its own base, and wherein there is a means for disposing the valve in the container inside of the applicator. Examples of these applicator devices are described in U.S. Patents 4,693,623 to Schwartzman; issued September 25, 1987; 3,669,323; Harker et al.; issued June 13, 1972; 3,418,055; Schwartzman; issued December 24, 1968; and 3,410,645; Schwartzman; issued November 12, 1968; Examples of applicators useful

herein are commercially available from Dab-O-Matic, Mount Vernon, N.Y.

[0125] Topical compositions of the present invention can also be delivered via conventional hair care products, including, but not limited to shampoos, conditioners, styling products or other leave-in or rinse off products.

5 EXAMPLES

[0126] Example 1-5 are nonlimiting examples of topical compositions used in the method of the present invention:

10	Ingredient	Example 1 (% by weight)	Example 2 (% by weight)	Example 3 (% by weight)	Example 4 (% by weight)	Example 5 (% by weight)
	Betulinic acid	5.0	0.0	3.0	3.0	3.0
	Betulonic Acid	0.0	3.0	0.0	0.0	0.0
	Minoxidil	0.0	0.0	0.0	0.0	2.0
15	Tween 20	1.0	0.0	0.20	0.0	0.0
	isopropyl alcohol	47.0	48.5	48.5	48.5	47.5
	propylene glycol	28.2	29.1	29.1	29.1	28.5
	dimethylisosorbide	18.8	19.4	0.0	18.9	18.1
20	C ₁₂ -C ₁₅ alkyl octanoate	0.0	0.0	19.1	0.0	0.0
	hydroxypropyl cellulose	0.0	0.0	0.10	0.0	0.0
	polyquaternium 10	0.0	0.0	0.0	0.50	1.0
25	Total	100.0	100.0	100.0	100.0	100.0

Example 1 is prepared as follows:

[0127]

30 1. Add the isopropyl alcohol and Tween 20 into mixing container and agitate until combined.
 2. Add betulinic acid into the isopropyl alcohol and Tween solution and mix with a high shear mixer for 10 minutes.
 3. Add the remaining ingredients and mix an additional 10 minutes.

35 Example 2 is prepared as follows:

[0128]

40 1. Combine the isopropyl alcohol, propylene glycol and dimethylisosobide into mixing container and mix until in a clear solution.
 2. Add the betulonic acid to the combined solution and mix until in a clear solution.

Example 3 is prepared as follows:

45 [0129]

50 1. Add the isopropyl alcohol and Tween 20 into mixing container and agitate until combined.
 2. Add betulinic acid into the isopropyl alcohol and Tween solution and mix with a high shear mixer for 10 minutes.
 3. Add the propylene glycol and C₁₂-C₁₅ alkyl octanoate to the mixture and mix an additional 10 minutes.
 4. Add in the hydroxypropyl cellulose to the mixture and mix with a standard mixer for 4 to 5 hours.

Examples 4 and 5 are prepared as follows:

[0130]

55 1. Add the isopropyl alcohol and polyquaternium 10 into mixing container and mix for 1 to 2 hours.
 2. Add betulinic acid into the isopropyl alcohol and polyquaternium 10 mixture and mix with a high shear mixer for 10 minutes.

3. Add the remaining ingredients and mix an additional 10 minutes.

Examples 6 and 7 are nonlimiting examples of tablet compositions which can be used in the method of the present invention:

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Example 6 is prepared as follows:

[0131]

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1. Add the betulinic acid, the crospovidone and the microcrystalline cellulose into a twin-shell blender and mix for 20 minutes.
2. Sieve the mixture through a 40 mesh screen and return to the twin-shell blender.
3. Add the lactose hydrous and mix for 25 minutes.
4. Add the magnesium stearate and mix for 5 minutes.
5. Compress into tablets on a standard rotary tablet press.

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Example 7 is prepared as follows:

[0132]

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1. Dissolve the betulinic acid and polyvinylpyrrolidone in the methanol under agitation.
2. Add the sodium starch glycolate, dicalcium phosphate, and starch 1500 into a high shear mixer and mix for 15 minutes.
3. Add the methanol solution to the high-shear blender over a 10 minute period and then mix for an additional 10 minutes until granules are formed.
4. Transfer the wetted mass into a fluid bed dryer and dry at 45°C for 2 hours.
5. Sieve the dried granules through a 30 mesh screen and transfer back to the high-shear blender.
6. Add the talc and magnesium stearate and mix for 3 minutes.
7. Compress into tablets on a standard rotary tablet press

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Example 8 is a nonlimiting example of a composition which can be injected subcutaneously according to the method of the present invention.

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Ingredient	Example 6 (mg)	Example 7 (mg)
Betulinic acid	100	0.25
Crospovidone	15	0.0
Lactose, hydrous	200	0.0
Microcrystalline cellulose	80	0.0
Magnesium stearate	5	2.0
Polyvinylpyrrolidone	0.0	3.0
Sodium starch glycolate	0.0	2.0
Dicalcium phosphate	0.0	75.0
Talc	0.0	2.75
Methanol	0.0	20.0
Starch 1500	0.0	15.0

Ingredient	Example 8 (mg/mL)
Betulinic acid	1.0
Dibasic sodium phosphate	7.0
Monobasic sodium phosphate	3.0
Edetate disodium	0.1
Benzalkonium chloride	0.1
Water for injection	QS to 10 liters

Example 8 is prepared as follows:

[0133]

- 5 1. The betulinic acid is micronized in a jet mill and sterilized by exposing it to 2.5 Mrad of radiation from a cobalt 60 source.
2. The dibasic sodium phosphate, monobasic sodium phosphate, edetate disodium, and benzalkonium chloride are dissolved in 9 liters of water for injection in a standard mixing tank.
- 10 3. The solution is filtered through a 0.22 micron filter to achieve sterilization.
4. The betulinic acid is added and mixed for 30 minutes under agitation.
5. The suspension is aseptically filled into 3 mL flint glass vials, stoppered and sealed on standard filling equipment.

Claims

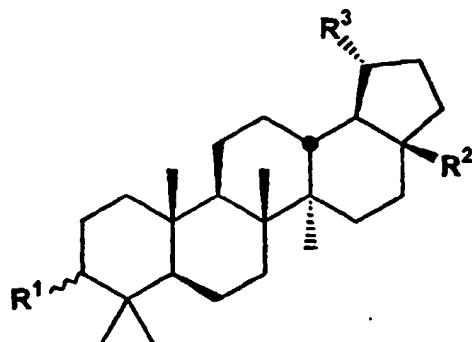
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1. A cosmetic method for regulating hair growth comprising the administration to a human of a composition comprising about 0.00001% to about 99.9% of a compound selected from the group consisting of:

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- a) lupane triterpenes having the structure:

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Where R¹ is either

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- 1) connected to the ring system via a single bond, either α - or β -configuration, and is selected from the group consisting of: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; halogen where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;
- 2) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R⁴,

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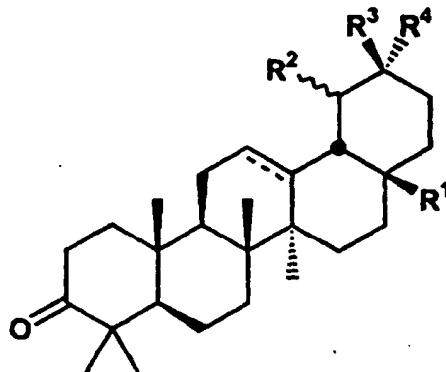
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Where R² is selected from the group consisting of: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or

without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv) , OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂; and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

And where R³ is selected from the group consisting of C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵, or C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, where R⁵ is selected from the group consisting of OH and a halogen,

b) compounds having the structure:



where R₁ is selected from the following groups: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNHR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of 1) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: a) halogens, b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ c) OH, d), OR⁴, e) OCOR⁴, f) OCOOR⁴, g) OCONHR⁴, or h) OCON(R⁴)₂ and 2) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

where R₂ = CH₃ or H,

where R₃ = CH₃ or H, and

where R₄ = CH₃ or H; and

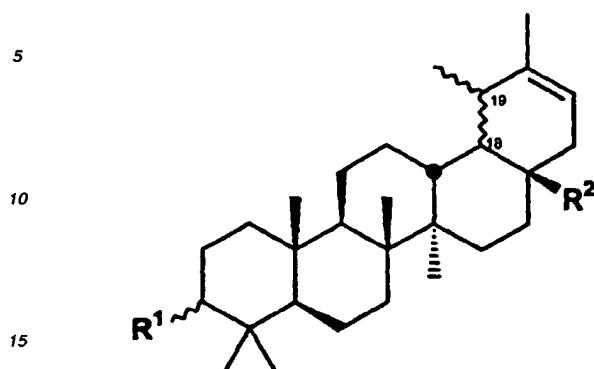
c) compounds having the structure:

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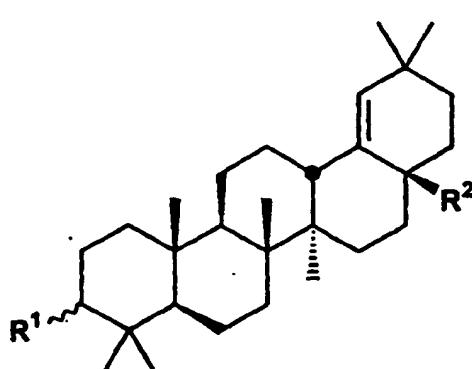
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i)



ii)

Where R¹ is either

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1) connected to the ring system via a single bond, either α - or β - configuration, and is selected from the group consisting of: H, OH, R⁴, OR⁴, OCOR⁴, OCONHR⁴, or OCON(R⁴)₂; halogen where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain , saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv) , OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂, or

2) connected to the ring system via a double bond and is selected from the group consisting of a)oxygen, b) sulfur and c) R⁴, and

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Where R² is selected from the group consisting of: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain , saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstitued aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv), OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂

d) salts of the acid forms of (a), (b) or (c); and

e) mixtures of (a), (b), (c) or (d).

50 2. The method of Claim 1 wherein the composition is administered via the topical application of the composition to the scalp.

3. The method of Claim 2 wherein the compound is selected from the group consisting of betulinic acid, betulonic acid and mixtures thereof.

55 4. The method of Claim 3 wherein the compound is betulinic acid.

5. The method of Claim 3 wherein the compound is betulonic acid.

6. The method of Claim 1 wherein the composition additionally comprises a cosmetically or pharmaceutically acceptable vehicle.

5 7. The method of Claim 6 wherein the cosmetically or pharmaceutically acceptable vehicle is present at a level ranging from about 50% to about 99.999% by weight of the composition.

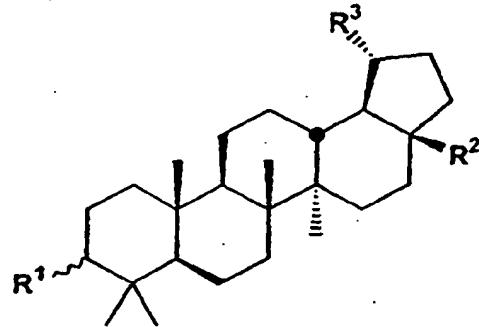
10 8. The method of Claim 7 which additionally comprises a second hair growth agent selected from the group consisting of zinc salts of carboxylic acids, saponins, other triterpenes such as oleanolic acid and ursolic acid, crataegolic acid, celastrol, asiatic acid, inhibitors of 5- α -reductase such as progesterone, 1,4-methyl-4-azasteroids, in particular 17- β -N,N-diethylcarbamoyl-4-methyl-4-aza-5- α -androstan-3-one, androgen receptor antagonists such as cyproterone acetate, Minoxidil azelaic acid and its derivatives, cyclosporin, triiodothyronine, diazoxide, potassium channel openers such as cromakalin, phenytoin and mixtures thereof.

15 9. The method of Claim 2 wherein the composition is applied to the scalp where the hair is bald or balding.

10 10. The method of Claim 9 wherein the composition is topically applied from 1 to about 10 times per day.

20 11. Use of a composition comprising about 0.00001% to about 99.9% of a compound selected from the group consisting of:

25 a) lupane triterpenes having the structure:



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35 Where R¹ is either

40 1) connected to the ring system via a single bond, either α - or β - configuration, and is selected from the group consisting of: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; halogen where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

45 2) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R⁴,

50 55 Where R² is selected from the group consisting of: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups contain-

ing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; iii) OH, iv) , OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂; and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

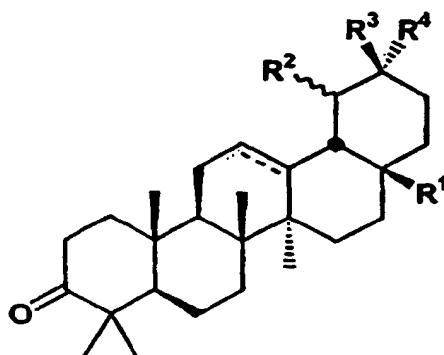
10 And where R³ is selected from the group consisting of C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵, or C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, where R⁵ is selected from the group consisting of OH and a halogen,

b) compounds having the structure:

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where R₁ is selected from the following groups: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of 1) cyclic, straight chain or branched chain, saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: a) halogens, b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂; c) OH, d) , OR⁴, e) OCOR⁴, f) OCOOR⁴, g) OCONHR⁴, or h) OCON(R⁴)₂ and 2) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

where R₂ = CH₃ or H,

where R₃ = CH₃ or H, and

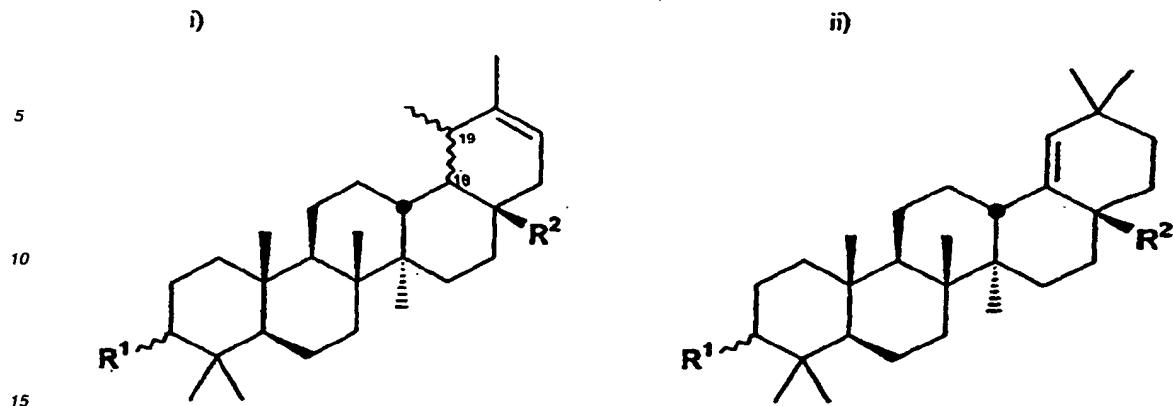
where R₄ = CH₃ or H; and

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c) compounds having the structure:

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Where R¹ is either

20 1) connected to the ring system via a single bond, either α - or β - configuration, and is selected from the group consisting of: H, OH, R⁴, OR⁴, OCOR⁴, OCONHR⁴, or OCON(R⁴)₂; halogen where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain , saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted; is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂ and b) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂;

25 2) connected to the ring system via a double bond and is selected from the group consisting of a) oxygen, b) sulfur and c) R⁴, and

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Where R² is selected from the group consisting of: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴ where R⁴ is independently selected from the group consisting of a) cyclic, straight chain or branched chain , saturated or unsaturated, substituted or unsubstituted alkyl groups containing from 1-20 carbons, where the alkyl group, if substituted, is substituted with a substituent selected from the group consisting of: i) halogens, ii) substituted or unsubstituted aryl groups comprising from 1 to 5 rings with or without heteroatoms, which heteroatoms are selected from the group consisting of nitrogen, oxygen or sulfur, where the aryl group, if substituted, is substituted with a substituent selected from the group consisting of halogens, alkyl groups, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, or OCON(R⁴)₂ iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, or viii) OCON(R⁴)₂.

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d) salts of the acid forms of (a), (b) or (c); and
e) mixtures of (a), (b), (c) or (d);

for the preparation of a medicament for regulating hair growth.

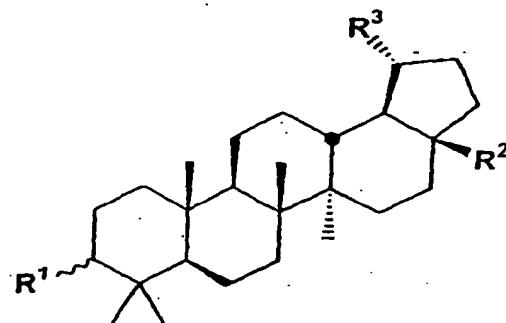
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Patentansprüche

1. Kosmetisches Verfahren zum Regulieren des Haarwachstums, umfassend die Verabreichung einer Zusammensetzung an einen Menschen, die Zusammensetzung ungefähr 0,00001% bis ungefähr 99,9% einer Verbindung umfassend, die ausgewählt ist aus der Gruppe bestehend aus:

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a) Lusan-Triterpene mit der Struktur:



worin R¹ entweder

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1) mit dem Ringsystem mittels einer Einfachbindung verknüpft ist, entweder in der α - oder der β - Konfiguration, und ausgewählt ist aus der Gruppe bestehend aus: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂; Halogen, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCONC(R⁴)₂, und b) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, oder

2) mit dem Ringsystem mittels einer Doppelbindung verknüpft ist und ausgewählt ist aus der Gruppe bestehend aus a) Sauerstoff, b) Schwefel und c) R⁴,

worin R² ausgewählt ist aus der Gruppe bestehend aus: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCON(R⁴)₂, und b) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂; und worin R³ ausgewählt ist aus der Gruppe bestehend aus C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵ oder C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, worin R⁵ ausgewählt ist aus der Gruppe bestehend aus OH und einem Halogen,

b) Verbindungen mit der Struktur:

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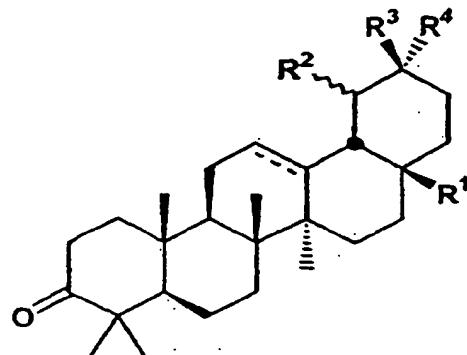
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worin R^1 ausgewählt ist aus den folgenden Gruppen: CH_3 , CH_2OH , CH_2OR^4 , CHO , CO_2H , CO_2R^4 , $COHNR^4$, $CON(R^4)_2$, CH_2OCOR^4 , worin R^4 unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus 1) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht Substitutionen Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: a) Halogenen, b) substituierten oder nicht substituierten Arylgruppen, umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR^4 , $OCOR^4$, $OCOOR^4$, $OCONHR^4$ oder $OCON(R^4)$, c) OH, d) OR^4 , e) $OCOR^4$, f) $OCOOR^4$, g) $OCONHR^4$ oder h) $OCON(R^4)_2$, und 2) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR^4 , $OCOR^4$, $OCOOR^4$, $OCONHR^4$ oder $OCON(R^4)_2$;

worin $R^2 = CH_3$ oder H,
worin $R^3 = CH_3$ oder H, und
worin $R^4 = CH_3$ oder H ist; und

c) Verbindungen mit der Struktur:

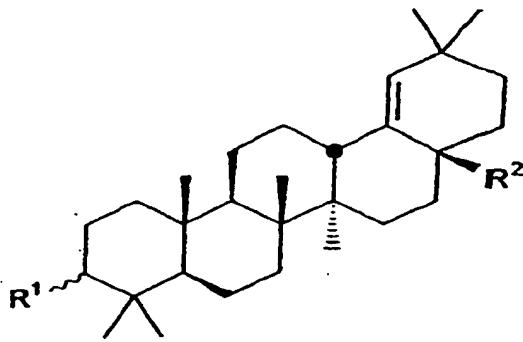
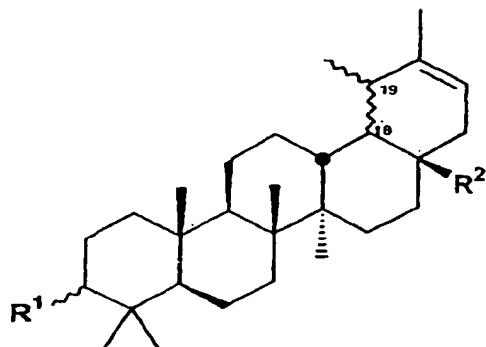
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ii).



worin R^1 entweder

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1) mit dem Ringsystem mittels einer Einfachbindung verknüpft ist, entweder in der α - oder der β - Konfiguration, und ausgewählt ist aus der Gruppe bestehend aus: H, OH, R^4 , OR^4 , $OCOR^4$, $OCOOR^4$, $OCONHR^4$ oder $OCON(R^4)_2$; Halogen, worin R^4 unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substitu-

ierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCON(R⁴)₂, und b) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, oder

5 2) mit dem Ringsystem mittels einer Doppelbindung verknüpft ist und ausgewählt ist aus der Gruppe bestehend aus a) Sauerstoff, b) Schwefel und c) R⁴, und

10 15 worin R² ausgewählt ist aus der Gruppe bestehend aus: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴), iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCON(R⁴)₂

20 25 d) Salze der Säureformen von (a), (b) oder (c); und

30 e) Mischungen aus (a), (b), (c) oder (d).

35 2. Verfahren nach Anspruch 1, worin die Zusammensetzung mittels der topischen Aufbringung der Zusammensetzung auf die Kopfhaut verabreicht wird.

40 3. Verfahren nach Anspruch 2, worin die Verbindung ausgewählt ist aus der Gruppe bestehend aus Betulinsäure, Betulonsäure (betulonic acid) und Mischungen daraus.

45 4. Verfahren nach Anspruch 3, worin die Verbindung Betulinsäure ist.

5. Verfahren nach Anspruch 3, worin die Verbindung Betulonsäure ist.

50 6. Verfahren nach Anspruch 1, worin die Zusammensetzung zusätzlich ein kosmetisch oder pharmazeutisch akzeptables Vehikel umfaßt.

7. Verfahren nach Anspruch 6, worin das kosmetisch oder pharmazeutisch akzeptable Vehikel in einer Menge von ungefähr 50% bis ungefähr 99,999%, bezogen auf das Gewicht der Zusammensetzung, vorhanden ist.

55 8. Verfahren nach Anspruch 7, welches zusätzlich ein zweites Haarwuchsmittel umfaßt, ausgewählt aus der Gruppe bestehend aus Zinksalzen von Carbonsäuren, Saponinen, weiteren Triterpenen, wie Oleanolsäure und Ursolsäure, Crataegolsäure, Celastrol, Asiatsäure, Inhibitoren der 5- α -Reduktase, wie Progesteron, 1,4-Methyl-4-azasteroide, insbesondere 17- β -N,N-Diethylcarbamoyl-4-methyl-4-aza-5- α -androstan-3-on, Androgenrezeptor-Antagonisten, wie Cyproteronacetat, Minoxidil, Azelainsäure und ihre Derivate, Cyclosporin, Triiodothyronin, Diazoxid, Kaliumkanal-Öffner, wie Cromakalin, Phenytoin und Mischungen daraus.

9. Verfahren nach Anspruch 2, worin die Zusammensetzung auf die Kopfhaut aufgebracht wird, deren Haar verschwunden ist oder sich ausdünnnt.

10. Verfahren nach Anspruch 9, worin die Zusammensetzung topisch 1 bis ungefähr 10 mal pro Tag aufgebracht wird.

11. Verwendung einer Zusammensetzung umfassend ungefähr 0,00001% bis ungefähr 99,9% einer Verbindung ausgewählt aus der Gruppe bestehend aus:

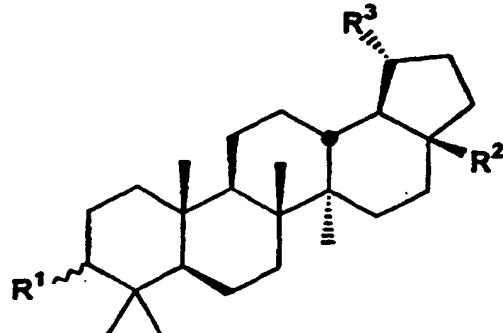
a) Lusan-Triterpenen mit der Struktur:

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worin R¹ entweder

25 1) mit dem Ringsystem mittels einer Einfachbindung verknüpft ist, entweder in der α - oder der β - Konfiguration, und ausgewählt ist aus der Gruppe bestehend aus: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂; Halogen, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCONC(R⁴)₂, und b) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, oder

30 2) mit dem Ringsystem mittels einer Doppelbindung verknüpft ist und ausgewählt ist aus der Gruppe bestehend aus a) Sauerstoff, b) Schwefel und c) R⁴,

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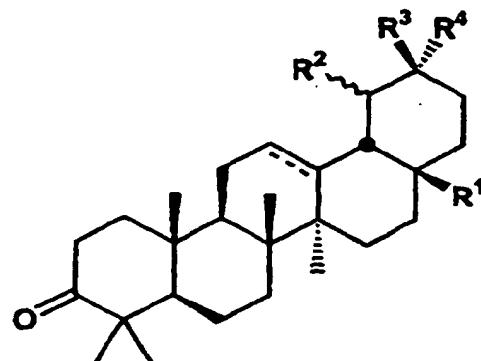
worin R² ausgewählt ist aus der Gruppe bestehend aus: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCON(R⁴)₂, und b) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂; und worin R³ ausgewählt ist aus der Gruppe bestehend aus C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵ oder C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, worin R⁵ ausgewählt ist aus der Gruppe be-

stehend aus OH und einem Halogen,

b) Verbindungen mit der Struktur:

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worin R¹ ausgewählt ist aus den folgenden Gruppen: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus 1) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: a) Halogenen, b) substituierten oder nicht substituierten Arylgruppen, umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴), c) OH, d) OR⁴, e) OCOR⁴, f) OCOOR⁴, g) OCONHR⁴ oder h) OCON(R⁴)₂; und 2) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂;

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worin R² = CH₃ oder H,
worin R³ = CH₃ oder H, und
worin R⁴ = CH₃ oder H ist; und

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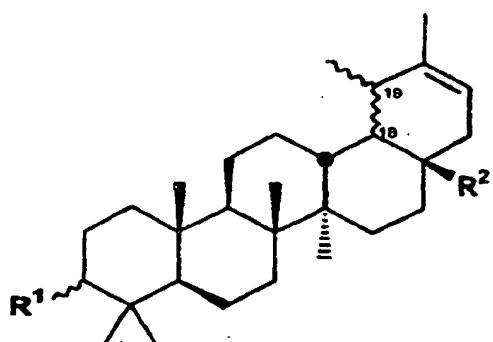
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c) Verbindungen mit der Struktur:

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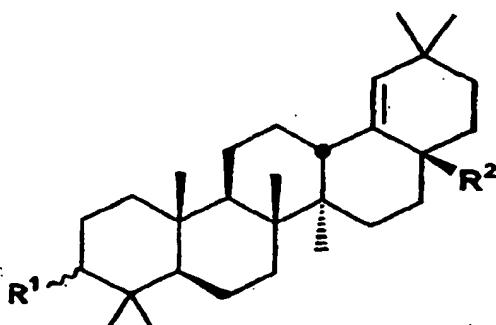
i)

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ii)

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worin R¹ entweder

1) mit dem Ringsystem mittels einer Einfachbindung verknüpft ist, entweder in der α - oder der β - Konfiguration, und ausgewählt ist aus der Gruppe bestehend aus: H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂: Halogenen, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCON(R⁴)₂, und b) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, oder

2) mit dem Ringsystem mittels einer Doppelbindung verknüpft ist und ausgewählt ist aus der Gruppe bestehend aus a) Sauerstoff, b) Schwefel und c) R⁴, und

worin R² ausgewählt ist aus der Gruppe bestehend aus: CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, worin R⁴ unabhängig voneinander ausgewählt ist aus der Gruppe bestehend aus a) zyklischen, geradkettigen oder verzweigten, gesättigten oder ungesättigten, substituierten oder nicht substituierten Alkylgruppen enthaltend 1 - 20 Kohlenstoffatome, worin die Alkylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus: i) Halogenen, ii) substituierten oder nicht substituierten Arylgruppen umfassend 1 bis 5 Ringe, mit oder ohne Heteroatome, wobei die Heteroatome ausgewählt sind aus der Gruppe bestehend aus Stickstoff, Sauerstoff oder Schwefel, worin die Arylgruppe, falls sie substituiert ist, mit einem Substituenten substituiert ist ausgewählt aus der Gruppe bestehend aus Halogenen, Alkylgruppen, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴ oder OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴ oder viii) OCON(R⁴)₂

d) Salze der Säureformen von (a), (b) oder (c); und

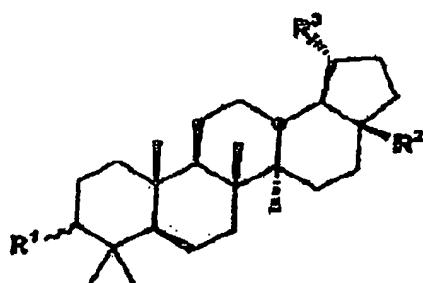
e) Mischungen aus (a), (b), (c) oder (d).

zur Herstellung eines Medikamentes zur Regulierung des Haarwachstums.

Revendications

1. Procédé cosmétique pour le contrôle de la poussée des cheveux, comprenant l'administration à une personne d'une composition comprenant d'environ 0,00001% à environ 99,9% d'un composé choisi dans le groupe constitué par :

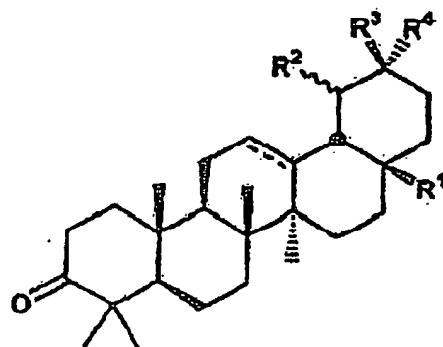
a) les triterpènes de lupane ayant la structure :



dans laquelle R¹ est soit

1) connecté au système cyclique au moyen d'une simple liaison, selon une configuration α ou β , et est choisi dans le groupe constitué par H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂ : un halogène, dans lequel R⁴ est indépendamment choisi dans le groupe constitué par a) les groupes alkyles, substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, ou viii) OCON(R⁴)₂ et b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂ ou
2) connecté au système cyclique au moyen d'une liaison double et est choisi dans le groupe constitué par a) l'oxygène, b) le soufre et c) R⁴,

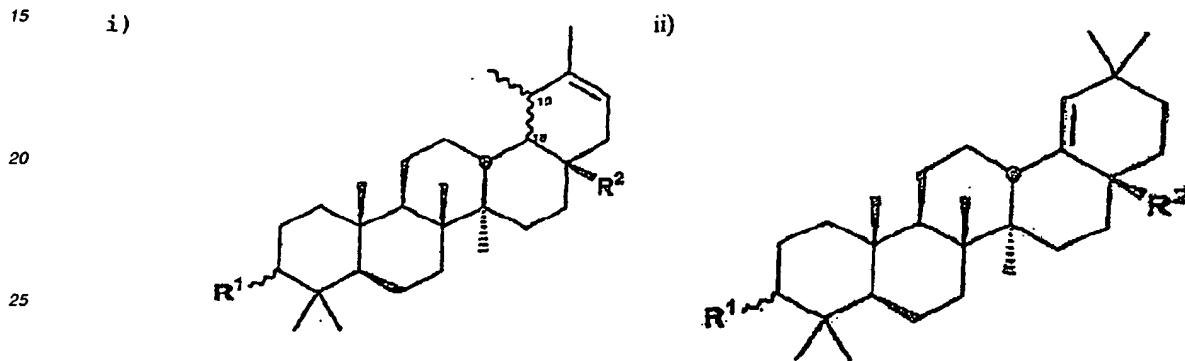
dans laquelle R² est choisi dans le groupe constitué par CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, dans lesquels R⁴ est choisi indépendamment dans le groupe constitué par
 20 a) les groupes alkyles, substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis
 25 dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOP⁴, vi) OCOOR⁴, vii) OCONHR⁴, ou viii) OCON(R⁴)₂; et b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe
 30 constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂ ; et dans laquelle R³ est choisi dans le groupe constitué par C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵, ou C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, dans lesquels R⁵ est choisi dans le groupe constitué par OH et un halogène,
 35 b) les composés ayant la structure :



55 dans laquelle R¹ est choisi parmi les groupes suivants : CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, dans lesquels R⁴ est choisi indépendamment dans le groupe constitué par 1) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : a) les halogènes, b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans des hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est

substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, c) OH, d) OR⁴, e) OCOR⁴, f) OCOOR⁴, g) OCONHR⁴, ou h) OCON(R⁴)₂ et 2) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂;

5 dans laquelle R₂ = CH₃ ou H,
 dans laquelle R₃ = CH₃ ou H, et
 10 dans laquelle R₄ = CH₃ ou H, et
 c) les composés ayant la structure :



30 où R¹ est soit

35 1) connecté au système cyclique au moyen d'une simple liaison, selon une configuration α ou β , et est choisi dans le groupe constitué par H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂; un halogène, dans lequel R⁴ est choisi indépendamment dans le groupe constitué par a) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, ou viii) OCON(R⁴)₂ et b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, ou

40 2) connecté au système cyclique au moyen d'une liaison double et est choisi dans le groupe constitué par a) l'oxygène, b) le soufre et c) R⁴; et

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50 dans laquelle R² est choisi dans le groupe constitué par CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, dans lesquels R⁴ est choisi indépendamment dans le groupe constitué par a) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴,

ou viii) OCON(R⁴)₂,
d) les sels des formes acides de (a), (b) ou (c) ; et
e) les mélanges de (a), (b), (c) ou (d).

5 2. Procédé selon la revendication 1 dans lequel la composition est administrée par application topique de la composition sur le cuir chevelu.

10 3. Procédé selon la revendication 2 dans lequel le composé est choisi dans le groupe constitué par l'acide bétulinique, l'acide bétulonique et les mélanges de ceux-ci.

15 4. Procédé selon la revendication 3 dans lequel le composé est l'acide bétulinique.

20 5. Procédé selon la revendication 3 dans lequel le composé est l'acide bétulonique.

25 6. Procédé selon la revendication 1 dans lequel la composition comprend également un véhicule cosmétiquement ou pharmaceutiquement acceptable.

30 7. Procédé selon la revendication 6 dans lequel le véhicule cosmétiquement ou pharmaceutiquement acceptable est présent à un taux allant d'environ 50% à environ 99,999% en poids de la composition.

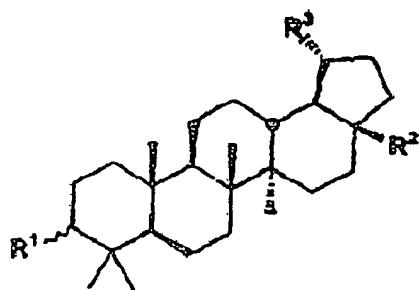
35 8. Procédé selon la revendication 7 comprenant en outre un deuxième agent de pousse des cheveux choisi dans le groupe constitué par les sels de zinc d'acides carboxyliques, les saponines, d'autres triterpènes tels que l'acide oléanolique et l'acide ursolique, l'acide crataégolique, le célastrol, l'acide asiatique, les inhibiteurs de la 5- α -réductase tels que la progestérone, les 1,4-méthyl-4-azastéroïdes, en particulier le 17- β -N,N-diéthylcarbamoyl-4-méthyl-4-aza-5- α -androstan-3-one, les antagonistes des récepteurs aux androgènes tels que l'acétate de cyprotérone, le minoxidil, l'acide azélaïque et ses dérivés, la cyclosporine, la triiodothyronine, le diazoxyde, les ouvreurs de canaux potassiques tels que la cromakaline, la phénytoïne et les mélanges de ceux-ci.

40 9. Procédé selon la revendication 2 dans lequel la composition est appliquée sur le cuir chevelu dans les zones de calvitie ou en cours de calvitie.

45 10. Procédé selon la revendication 9 dans lequel la composition est appliquée par voie topique de 1 à environ 10 fois par jour.

50 11. Utilisation d'une composition comprenant d'environ 0,00001% à environ 99,9% d'un composé choisi dans le groupe constitué par :

a) les triterpènes de lupane ayant la structure :

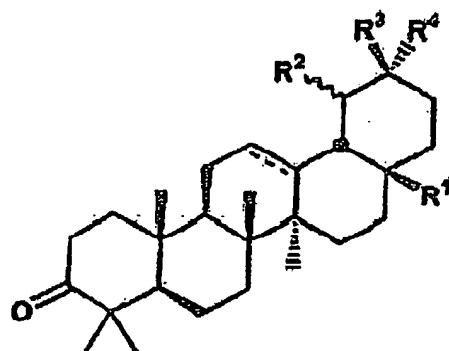


dans laquelle R¹ est soit

55 1) connecté au système cyclique au moyen d'une simple liaison, selon une configuration α ou β , et est choisi dans le groupe constitué par H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂; un halogène, dans lequel R⁴ est choisi indépendamment dans le groupe constitué par a) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée,

comportant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, ou viii) OCON(R⁴)₂ et b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, ou
10 2) connecté au système cyclique au moyen d'une liaison double et est choisi dans le groupe constitué par a) l'oxygène, b) le soufre et c) R⁴ ;

15 dans laquelle R² est choisi dans le groupe constitué par CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, dans lesquels R⁴ est choisi indépendamment dans le groupe constitué par a) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, ou viii) OCON(R⁴)₂; et b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂ ;
20 et dans laquelle R³ est choisi dans le groupe constitué par C(CH₃)=CH₂, CH(CH₃)₂, COCH₃, CH(OH)CH₃, CH₂CH₃, C(R⁵)(CH₃)CH₂R⁵, ou C(CH₃)₂R⁵, CH(CH₃)CH₂R⁵, dans lesquels R⁵ est choisi dans le groupe constitué par OH et un halogène,
25 30 b) les composés ayant la structure suivante :

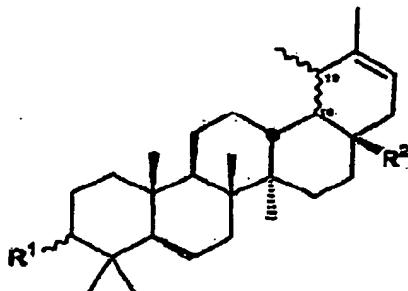


35 dans laquelle R¹ est choisi parmi les groupes suivants : CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, dans lesquels R⁴ est choisi indépendamment dans le groupe constitué par 40 1) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : a) les halogènes, b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, c) OH, d) OR⁴, e) OCOR⁴, f) OCOOR⁴, g) OCONHR⁴, ou h) OCON(R⁴)₂ et 45 2) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou

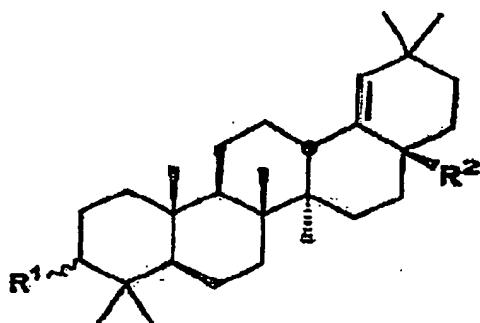
sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂ ;

5 dans laquelle R₂ = CH₃ ou H,
 dans laquelle R₃ = CH₃ ou H, et
 dans laquelle R₄ = CH₃ ou H, et
 c) les composés ayant la structure :

10 i)



ii)



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où R¹ est soit

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1) connecté au système cyclique au moyen d'une simple liaison, selon une configuration α ou β , et est choisi dans le groupe constitué par H, OH, R⁴, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂ ; un halogène, dans lequel R⁴ est choisi indépendamment dans le groupe constitué par a) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, ou viii) OCON(R⁴)₂ et b) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, ou
 30 2) connecté au système cyclique au moyen d'une liaison double et est choisi dans le groupe constitué par a) l'oxygène, b) le soufre et c) R⁴, et

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dans laquelle R² est choisi dans le groupe constitué par CH₃, CH₂OH, CH₂OR⁴, CHO, CO₂H, CO₂R⁴, COHNR⁴, CON(R⁴)₂, CH₂OCOR⁴, dans lesquels R⁴ est choisi indépendamment dans le groupe constitué par a) les groupes alkyles substitués ou non substitués, saturés ou insaturés, cycliques, à chaîne linéaire ou à chaîne ramifiée, comprenant de 1 à 20 carbones, dans lesquels le groupe alkyle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par : i) les halogènes, ii) les groupes aryles substitués ou non substitués comprenant de 1 à 5 noyaux avec ou sans hétéroatomes, lesquels hétéroatomes sont choisis dans le groupe constitué par l'azote, l'oxygène ou le soufre, dans lesquels le groupe aryle, s'il est substitué, est substitué par un substituant choisi dans le groupe constitué par les halogènes, les groupes alkyles, OH, OR⁴, OCOR⁴, OCOOR⁴, OCONHR⁴, ou OCON(R⁴)₂, iii) OH, iv) OR⁴, v) OCOR⁴, vi) OCOOR⁴, vii) OCONHR⁴, ou viii) OCON(R⁴)₂ ;
 d) les sels des formes acides de (a), (b) ou (c) ; et
 e) les mélanges de (a), (b), (c) ou (d),

pour la préparation d'un médicament destiné à la régulation de la pousse des cheveux.